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L4: Entry 27 of 32

File: USPT

US-PAT-NO: 5032552
DOCUMENT-IDENTIFIER: US 5032552 A

TITLE: Biomedical material

DATE-ISSUED: July 16, 1991

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Nonami; Tohru	Ichikawa			JP
Yasui; Nobuo	Narita			JP

US-CL-CURRENT: 501/95.3; 106/35, 501/1

CLAIMS:

We claim:

1. A biomedical material in the form a sintered composite body comprising a crystalline calcium phosphate matrix having a grain size of 0.05 to 30 .mu.m and inorganic whiskers having a length o 0.05 to 30 .mu.m and an aspect ratio as defined by the length/diameter of from 1.2/1 to 100/1, the ratio of matrix grain size to whisker length ranging from 10/1 to 1/10 dispersed therein, the whiskers occupying 0.5 to 95% by area of a cross section of the sintered body, and the inorganic whiskers being selected from the group consisting of calcium silicate, calcium aluminosilicate, calcium magnesium silicate, calcium aluminate, and magnesium silicate whiskers.

2. The biomedical material of claim 1 wherein the crystalline calcium phosphate is tricalcium phosphate.

3. The biomedical material of claim 1 wherein the crystalline calcium phosphate is an apatite.

4. The biomedical material of claim 3 wherein the crystalline calcium phosphate is hydroxyapatite or fluoroapatite having an atomic calcium-to-phosphorus (Ca/P) ratio of from 165/100 to 175/100.

5. The biomedical material of claim 1 wherein the inorganic

whiskers are selected from the group consisting of calcium aluminosilicate and calcium magnesium silicate whiskers.

6. The biomedical material of claim 5 wherein the inorganic whiskers are anorthite or diopside whiskers.

7. The biomedical material of claim 1, wherein an intermediate layer is present between the whiskers and the matrix grains, the intermediate layer containing at least one element present in either one or both of the whiskers and the matrix.

8. The biomedical material of claim 7 wherein the intermediate layer has a continuous or stepwise gradient of concentration and thickness of up to 3 .mu.m.

9. The biomedical material of claim 1 wherein the whiskers have a degree of orientation of at least 60%.

10. The biomedical material of claim 1, comprising 10-60% by weight of said inorganic whiskers per 100 parts by weight of said sintered body.

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L4: Entry 25 of 32 File: USPT

US-PAT-NO: 5125971
DOCUMENT-IDENTIFIER: US 5125971 A

TITLE: Living hard tissue replacement, its preparation

DATE-ISSUED: June 30, 1992

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Nonami; Tohru	Ichikawa			JP
Yasui; Nobuo	Narita			JP

US-CL-CURRENT: 106/35; 433/228.1, 501/1, 501/123, 501/154

CLAIMS:

We claim:

1. A living hard tissue replacement prepared by the superplastic forming of a ceramic material having crystalline grains which contains CaO and SiO.sub.2 as essential components, is substantially free from calcium phosphate, but capable of forming a calcium phosphate base compound upon contact with a phosphorus-containing aqueous solution.

2. The living hard tissue replacement of claim 1 wherein said ceramic material further contains MgO in addition of the essentia components CaO and SiO.sub.2.

3. The living hard tissue replacement of claim 2 wherein said ceramic material contains 10 to 90% by weight of CaO, 10 to 80% b weight of SiO.sub.2, and 0 to 35% by weight of MgO.

4. The living hard tissue replacement of claim 3 wherein said ceramic material has a composition selected from the group consisting of diopside, wollastonite, akermanite, monticellite, alite, and belite.

5. The living hard tissue replacement of claim 4 wherein said ceramic material contains at least 40% by volume of a diopside or wollastonite composition.

6. The living hard tissue replacement of claim 1 in the form of a artificial dental root or crown.

7. A method for preparing a living hard tissue replacement comprising the step of superplastic forming a ceramic material having crystalline grains which contains CaO and SiO.sub.2 as essential components, is substantially free from calcium phosphate, but capable of forming a calcium phosphate base compound upon contact with a phosphorus-containing aqueous solution.

8. The method of claim 7 wherein said ceramic material further contains MgO in addition of the essential components CaO and SiO.sub.2.

9. The method of claim 8 wherein said ceramic material contains 1 to 90% by weight of CaO, 10 to 80% by weight of SiO.sub.2, and 0 to 35% by weight of MgO.

10. The method of claim 9 wherein said ceramic material has a composition selected from the group consisting of diopside, wollastonite, akermanite, monticellite, alite, and belite.

11. The method of claim 10 wherein said ceramic material contains at least 40% by volume of a diopside or wollastonite composition.

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L4: Entry 24 of 32 File: USPT

US-PAT-NO: 5134009
DOCUMENT-IDENTIFIER: US 5134009 A

TITLE: Shaped article of oriented calcium phosphate type compounds, sinter thereof and processes for producing same

DATE-ISSUED: July 28, 1992

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ichitsuka; Takeshi	Tokyo			JP
Ogawa; Tetsuro	Tokyo			JP
Sumita; Masaya	Tokyo			JP
Yokoo; Akihiko	Tokyo			JP

US-CL-CURRENT: 428/113; 428/105, 428/221, 428/372, 428/373, 428/688, 428/704

CLAIMS:

What is claimed is:

1. An oriented shaped article of a calcium phosphate compound comprising primary particles of said calcium phosphate compound having at least two crystallographic axes, wherein at least two o said axes are oriented in one direction in at least a surface portion of said article.

2. An oriented shaped article of a calcium phosphate compound as claimed in claim 1, wherein said at least two of said axes are oriented in one direction i the entire article.

3. An oriented sinter of a calcium phosphate compound comprising primary particles of aid calcium phosphate compound having at least two crystallographic axes, wherein at least two of said axe are oriented in one direction in at least a surface portion of said sinter.

4. An oriented sinter of a calcium phosphate compound as claimed in claim 3, wherein at least two of said axes are oriented in one direction in the entire sinter.

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L4: Entry 24 of 32 File: USPT

DOCUMENT-IDENTIFIER: US 5134009 A
TITLE: Shaped article of oriented calcium phosphate type compounds, sinter thereof and processes for producing same

Abstract Text (1):
An oriented shaped article of a calcium phosphate type compound is disclosed, in which at least two crystallographic axes of the primary particles of which the shaped article is composed each is oriented in one direction, respectively, in at least the surface of said article. A sinte the oriented shaped article and a processes for producing the article and the sinter are also disclosed.

Brief Summary Text (2):
The present invention relates to shaped articles of calcium phosphate type compounds useful as biomaterials (e.g., artificial teeth and bones) as materials for humidity sensors, filters or IC substrates. The present invention also relates to sinters of these shaped articles and processes f producing the shaped articles and the sinters.

Brief Summary Text (4):
Due to their high biocompatibility, calcium phosphate type ceramics have conventionally been used as biomaterials such as artificial tooth ro and bones. Because the crystal particles (primary particles) of these ceramics are unoriented and these ceramics are unoriented polycrystallin bodies, the mechanical properties of these ceramics are isotropic. When these ceramics are placed under stress, the propagation of a fracture will travel over the shortest distance irrespective of the direction in which the stress is applied and the surface energy for a fracture becomes small that it will eventually cause a reduction in the fracture toughness of a shaped article of these ceramics and hence sinters thereof. Attem have been made to increase the strength of these ceramics by sintering them for high density after performing a suitable treatment such as HI (hot isotactic press), but no success has been achieved in improving their fracture toughness (as described, e.g., in Preprints of Annual Meeti of the Ceramics Society of Japan 1984, 3G10, pp. 939, published on May 14, 1984).

Brief Summary Text (5):
Hydroxyapatite which is in the class of calcium phosphate type compounds has ionic conductivity and research has been undertaken to study use as an electronic material in devices such as humidity sensors. However, conventional hydroxyapatite ceramics are also isotropic with res to electrical properties, and conduction ions in the ceramics are diffused at grain boundaries, making it impossible to provide satisfactory conductivity to the ceramics (As described, e.g., in Preprints of 2nd Apatite Meeting, pp. 22, published on Dec. 1, 1986).

Brief Summary Text (6):
In order to exploit the above various properties of calcium phosphate type ceramics in an advantageous way, it is necessary that shaped artic or sinters thereof have anisotropy. The ideal method for meeting this need would be to use single crystals of these ceramics. However, it is generally difficult to prepare large single crystals of calcium phosphate, and, in fact, no report has been published that describes success in preparing large single crystals of calcium phosphate.

Brief Summary Text (7):
In order to attain anisotropy for various properties of shaped articles and sinters, it is necessary that at least two crystallographic axes or at le two crystal faces each must be oriented in one direction, respectively. For example, in tubular bones of animals, the c axis of apatite crystals the bone is oriented in the direction parallel to the longitudinal direction of the bone, and the a axis thereof is oriented in the direction perpendicular to the longitudinal direction of the bone, by which the anisotropy of the mechanical properties is attained.

Brief Summary Text (8):
Hydroxyapatite sinters in which one crystal face of the crystalline particles is oriented by hot-pressing has been reported in Preprints of Annu Meeting of the Ceramic Society of Japan 1984, A-72, pp. 511, published on May 14, 1984. In this method, because tabular (plate-like) cryst are used, the (h00) plane is oriented in the pressing direction, but there is no research whether other planes (such as the (001) plane) are orien in one direction. Therefore, it is unknown whether sinters having anisotropy for mechanical properties are obtained by this method.

Brief Summary Text (10):
The present inventors therefore conducted intensive studies in order to develop calcium phosphate type ceramics in which the crystal grains

(i.e., the primary particles) are oriented in one direction and thus succeeded in reaching the present invention.

Brief Summary Text (11):
One object of the present invention is to provide a shaped article of an oriented calcium phosphate type compound.

Brief Summary Text (12):
Another object of the present invention is to provide a sinter of a shaped article of an oriented calcium phosphate type compound.

Brief Summary Text (15):
The present invention provides a shaped article of a calcium phosphate type compound in which at least two crystallographic axes of the primary particles which make up the shaped article each is oriented in one direction, respectively, in at least the surface of the article. Such orientation can be throughout the entire article.

Brief Summary Text (16):
Such an oriented shaped article of a phosphate type compound can be produced by a process which comprises mixing an organic binder and water or an organic solvent with a powdered calcium phosphate type compound comprising rod-shaped crystal grains extending in the direct of one crystallographic axis thereof, kneading the mixed components, and extruding the resulting clay-like composition in a specified directi to shape the composition.

Brief Summary Text (17):
The present invention also provides an oriented sinter of a calcium phosphate type compound in which at least two crystallographic axes of t primary particles which make up the sinter each is oriented in one direction, respectively, in at least the surface of the sinter. The entire sinte can be oriented.

Brief Summary Text (18):
Such an oriented sinter of a calcium phosphate type compound can be produced by a process comprising mixing an organic binder and wate an organic solvent with a powdered calcium phosphate type compound comprising rod-shaped crystal grains extending in the direction of on crystallographic axis, kneading the mixed components, extruding the resulting clay-like composition in a specified direction to shape the composition, thermally decomposing the organic binder, and firing the shaped article at a temperature of from 900.degree. to 1,400.degree. C

Detailed Description Text (2):
Examples of the calcium phosphate type compound of the present invention include hydroxyapatite, fluoroapatite, chloroapatite and tricalciu phosphate.

Detailed Description Text (3):
A commonly employed method for orienting grains in the direction of a certain crystallographic axis is by utilizing the electric or magnetic polarity of the grains. This method, however, is not highly effective in orienting the crystals of calcium phosphate type compounds because t polarity is rather low.

Detailed Description Text (4):
If calcium phosphate type compounds are synthesized by a wet method under properly selected conditions, it is possible to prepare rod-like crystal grains that are elongate in the direction of the c-axis as described in J. Am. Chem. Soc., Oct. 25, 1967, pp. 5535-5541. For instance, s grains can be synthesized by mixing a calcium compound with a phosphoric acid compound, the pH of the reaction solution being adjusted t either neutral or alkaline with the temperature held in the range of from 10.degree. to 100.degree. C. The ratio of the long axis to the short ax of the rod-like grains is preferably 1.1 or more, more preferably 1.5 or more, and particularly preferably 2.0 or more.

Detailed Description Text (7):
The secondary particles of a calcium phosphate type compound can be pulverized into primary particles when they are mixed with an organi binder and water or an organic solvent. If the slurry is not dried but is subjected to filtration, no secondary particles will form and the synthesized crystal grains may be directly used without being pulverized.

Detailed Description Text (8):
Therefore, in accordance with the present invention, the rod-shaped crystal grains of a calcium phosphate type compound are used as a starti powder, which is mixed with suitable amounts of a heat-decomposable organic binder and water or an organic solvent, as well as optionally with other additives such as a dispersant and a plasticizer. The ingredients are kneaded and the resulting clay-like composition is extruded to shape the same.

Detailed Description Text (16):
A slurry of hydroxyapatite synthesized by a conventional wet method (as described in J. Am. Chem. Soc., Oct. 25, 1967, pp. 5535-5541) wa spray-dried to make a powder having an average particle size of about 7 .mu.m. Observation under a scanning electron microscope showed t the powder was composed of spherical secondary particles which were dense agglomerations of elongate primary grains having a width of fr

200 to 500 .ANG. and length of about 1,000 .ANG.. These particles were calcined at 700.degree. C. for 4 hours and pulverized with a supersonic mill (product of Nippon Pneumatic Co., Ltd.) to obtain a fine powder having an average particle size of about 1 .mu.m. This fine powder (feed powder) was used as a starting material for the next shaping step.

Detailed Description Text (19):
The "degree of orientation" of hydroxyapatite as defined below is shown in Table 1 for each sample. As one can see from Table 1, the sinter the shaped articles prepared in Example 1 had the c-axis of the primary particles oriented in the direction of extrusion. However, the pulveriz products of these sinters showed no appreciable orientation and the relative intensities of individual diffraction lines were in accord with the data of ASTM 24-33.

Detailed Description Text (20):
The "degree of orientation" of hydroxyapatite as used herein is defined by ##EQU1## wherein I.sub.(300) is the diffraction intensity from th (300) face of a sample, and I.sub.(002) is the diffraction intensity from the (002) face of the sample. The ASTM value for I.sub.(300) /I.sub.(002) is 1.5.

Detailed Description Text (27):
A slurry containing 4% hydroxyapatite particles (based on total slurry weight) with a width of from 200 to 500 .ANG. and a length of about 1,000 .ANG. was obtained by a conventional wet method of synthesis (as described in J. Am. Chem. Soc., Oct. 25, 1967, pp. 5535-5541). T slurry was concentrated by filtration, and the following composition was obtained.

Detailed Description Text (28):
The composition containing the thus synthesized rod-shaped crystals of hydroxyapatite, a binder and water was spun by extrusion through an nozzle (diameter: 0.3 mm) at an air pressure of 900 mmH.sub.2 O according to JP-A-61-106166, and dried with hot air at 300.degree. C. to form a gauze-like shaped article. The dried article was sintered at 1,100.degree. C. for 4 hours and subjected to X-ray diffractiometry to chec for the occurrence of orientation. When an unpulverized sample of the gauze-like article was loaded in a glass sample holder, grain orientatio was observed in the same manner as in Examples 1 and 2.

Detailed Description Text (35):
An hydroxyapatite cylindrical molded article, which was molded, dried and degreased in the same manner as in Example 1, was fired at 1,100.degree. C. to obtain a siner. The sinter was cut in the direction parallel to the molding direction or in the direction perpendicular to the molding direction. The cut surfaces were polished and measured for X-ray diffraction scans. The X-ray diffraction scan for the cut surface parallel to the molding direction is shown in FIG. 7. The X-ray diffraction scan for the cut surface perpendicular to the molding direction is shown in FIG. 8. Separately, the sinter was pulverized in a mortar and measured for an X-ray diffraction scan which is shown in FIG. 9.

Detailed Description Text (39):
An hydroxyapatite plate-like molded article, which was molded, dried and degreased in the same manner as in Example 4, was fired at 1,100.degree. C. to obtain a sinter. From the measurement of X-ray diffraction scans, it was found that the sinter had the same orientation properties as in the sinter obtained in Example 4.

Detailed Description Text (52):
In accordance with the present invention, a certain crystallographic axis of the primary particles in at least the surface or the entire portion of shaped article to be produced can be oriented in one direction by a simple method. The shaped article of a calcium phosphate calcium compound or the sinter thereof which is produced by the present invention has grain orientation so that their mechanical, electrical and chem properties are sufficiently anisotropic to provide improved characteristics over conventional materials. Further, the shaped article and sinter thereof are improved in fracture toughness.

Detailed Description Paragraph Table (2):

Composition	Amount
Hydroxyapatite	40%
Water	50%
Pullulan	10%

CLAIMS:

1. An oriented shaped article of a calcium phosphate compound comprising primary particles of said calcium phosphate compound having a least two crystallographic axes, wherein at least two of said axes are oriented in one direction in at least a surface portion of said article.

2. An oriented shaped article of a calcium phosphate compound as claimed in claim 1, wherein said at least two of said axes are oriented in o direction i the entire article.

3. An oriented sinter of a calcium phosphate compound comprising primary particles of aid calcium phosphate compound having at least two crystallographic axes, wherein at least two of said axes are oriented in one direction in at least a surface portion of said sinter.

4. An oriented sinter of a calcium phosphate compound as claimed in claim 3, wherein at least two of said axes are oriented in one direction the entire sinter.

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L4: Entry 22 of 32 File: USPT

US-PAT-NO: 5240659
DOCUMENT-IDENTIFIER: US 5240659 A

TITLE: Process for producing shaped article of oriented calcium phosphate type compound

DATE-ISSUED: August 31, 1993

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ichitsuka; Takeshi	Tokyo			JP
Ogawa; Tetsuro	Tokyo			JP
Sumita; Masaya	Tokyo			JP
Yokoo; Akihiko	Tokyo			JP

US-CL-CURRENT: 264/639; 264/108, 264/109, 264/125, 264/645

CLAIMS:

What is claimed is:

1. A process for producing an oriented shaped article of a calciu phosphate compound, which process comprises: mixing an organic binder and water or an organic solvent with a powder of a calcium phosphate compound comprising rod-shaped crystal grains extending in the direction of one crystallographic axis thereof, kneading the mixed components, and extruding the resulting composition in specified direction to shape said composition.

2. The process of claim 1, wherein at least two crystallographic axes of primary particles of which said oriented shaped article i composed each is oriented in one direction, respectively, in at least the surface of said article.

3. The process of claim 2, wherein said at least two crystallographic axes of the primary particles of which said oriented shaped article is composed each is oriented in one direction, respectively, in the entire portion of said article.

4. The process of claim 1, wherein the calcium phosphate compound is hydroxyapatite.

5. The process of claim 1, where the extruding is extrusion

molding at a molding pressure of from 0.2 to 500 kg/cm.sup.2.

6. The process of claim 1, wherein the extruding is injection molding.at a molding pressure of from 500 to 3,000 kg/cm.sup.2.

7. The process of claim 1, wherein the composition which is extruded comprises hydroxyapatite, water, butyl alcohol, methyl cellulose, a wax emulsion and a stearic acid emulsion.

8. The process of claim 1, wherein the composition which is extruded comprises hydroxyapatite, butyl methacrylate, an ethylene-vinyl acetate copolymer, a wax emulsion, dibutyl phthalate and stearic acid.

9. A process for producing an oriented sinter of a calcium phosphate compound, which process comprises: mixing an organic binder and water or an organic solvent with powder of the calcium phosphate compound comprising rod-shaped crystal grains extending in the direction of one crystallographic axis thereof, kneading the mixed components, extruding the resulting composition in a specified direction to shape said composition, thermally decomposing the organic binder, and firing the shaped article at temperature of from 900.degree. to 1,400.degree. C.

10. The process of claim 9, wherein at least two crystallographic axes of primary particles of which said oriented shaped sinter is composed each is oriented in one direction, respectively, in at least the surface of said sinter.

11. The process of claim 10, wherein said at least two crystallographic axes of the primary particles of which said oriented shaped sinter is composed each is oriented in one direction, respectively, in the entire portion of said sinter.

12. The process of claim 9, wherein the calcium phosphate compoun is hydroxyapatite.

13. The process of claim 9, where the extruding is extrusion molding at a molding pressure of from 0.2 to 500 kg/cm.sup.2.

14. The process of claim 9, wherein the extruding is injection molding at a molding pressure of rom 500 to 3,000 kg/cm.sup.2.

15. The process of claim 9, wherein the composition which is extruded comprises hydroxyapatite, water, butyl alcohol, methyl cellulose, a wax emulsion and a stearic acid emulsion.

16. The process of claim 9, wherein the composition which is extruded comprises hydroxyapatite, butyl methacrylate, an ethylene-vinyl acetate copolymer, a wax emulsion, dibutyl phthalate and stearic acid.

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L4: Entry 22 of 32 File: USPT

DOCUMENT-IDENTIFIER: US 5240659 A
TITLE: Process for producing shaped article of oriented calcium phosphate type compound

Abstract Text (1):
An oriented shaped article of a calcium phosphate type compound is disclosed, in which at least two crystallographic axes of the primary particles of which the shaped article is composed each is oriented in one direction, respectively, in at least the surface of said article. A sinte the oriented shaped article and a processes for producing the article and the sinter are also disclosed.

Brief Summary Text (2):
The present invention relates to shaped articles of calcium phosphate type compounds useful as biomaterials (e.g., artificial teeth and bones) as materials for humidity sensors, filters or IC substrates. The present invention also relates to sinters of these shaped articles and processes f producing the shaped articles and the sinters.

Brief Summary Text (4):
Due to their high biocompatibility, calcium phosphate type ceramics have conventionally been used as biomaterials such as artificial tooth ro and bones. Because the crystal particles (primary particles) of these ceramics are unoriented and these ceramics are unoriented polycrystallin bodies, the mechanical properties of these ceramics are isotropic. When these ceramics are placed under stress, the propagation of a fracture will travel over the shortest distance irrespective of the direction in which the stress is applied and the surface energy for a fracture becomes small that it will eventually cause a reduction in the fracture toughness of a shaped article of these ceramics and hence sinters thereof. Attem have been made to increase the strength of these ceramics by sintering them for high density after performing a suitable treatment such as HI (hot isotactic press), but no success has been achieved in improving their fracture toughness (as described, e.g., in Preprints of Annual Meeti of the Ceramics Society of Japan 1984, 3G10, pp. 939, published on May 14, 1984).

Brief Summary Text (5):
Hydroxyapatite which is in the class of calcium phosphate type compounds has ionic conductivity and research has been undertaken to study use as an electronic material in devices such as humidity sensors. However, conventional hydroxyapatite ceramics are also isotropic with res to electrical properties, and conduction ions in the ceramics are diffused at grain boundaries, making it impossible to provide satisfactory conductivity to the ceramics (As described, e.g., in Preprints of 2nd Apatite Meeting, pp. 22, published on Dec. 1, 1986).

Brief Summary Text (6):
In order to exploit the above various properties of calcium phosphate type ceramics in an advantageous way, it is necessary that shaped artic or sinters thereof have anisotropy. The ideal method for meeting this need would be to use single crystals of these ceramics. However, it is generally difficult to prepare large single crystals of calcium phosphate, and, in fact, no report has been published that describes success in preparing large single crystals of calcium phosphate.

Brief Summary Text (7):
In order to attain anisotropy for various properties of shaped articles and sinters, it is nessesary that at least two crystallographic axes or at le two crystal faces each must be oriented in one direction, respectively. For example, in tubular bones of animals, the c axis of apatite crystals the bone is oriented in the direction parallel to the longitudinal direction of the bone, and the a axis thereof is oriented in the direction perpendicular to the longitudinal direction of the bone, by which the anisotropy of the mechanical properties is attained.

Brief Summary Text (8):
Hydroxyapatite sinters in which one crystal face of the crystalline particles is oriented by hot-pressing has been reported in Preprints of Annu Meeting of the Ceramic Society of Japan 1984, A-72, pp. 511, published on May 14, 1984. In this method, because tabular (platelike) crysta are used, the (h00) plane is oriented in the pressing direction, but there is no research whether other planes (such as the (001) plane) are orien in one direction. Therefore, it is unknown whether sinters having anisotropy for mechanical properties are obtained by this method.

Brief Summary Text (10):
The present inventors therefore conducted intensive studies in order to develop calcium phosphate type ceramics in which the crystal grains

(i.e., the primary particles) are oriented in one direction and thus succeeded in reaching the present invention.

Brief Summary Text (11):
One object of the present invention is to provide a shaped article of an oriented calcium phosphate type compound.

Brief Summary Text (12):
Another object of the present invention is to provide a sinter of a shaped article of an oriented calcium phosphate type compound.

Brief Summary Text (15):
The present invention provides a shaped article of a calcium phosphate type compound in which at least two crystallographic axes of the primary particles which make up the shaped article each is oriented in one direction, respectively, in at least the surface of the article. Such orientation can be throughout the entire article.

Brief Summary Text (16):
Such an oriented shaped article of a phosphate type compound can be produced by a process which comprises mixing an organic binder and water or an organic solvent with a powdered calcium phosphate type compound comprising rod-shaped crystal grains extending in the direct of one crystallographic axis thereof, kneading the mixed components, and extruding the resulting clay-like composition in a specified directi to shape the composition.

Brief Summary Text (17):
The present invention also provides an oriented sinter of a calcium phosphate type compound in which at least two crystallographic axes of t primary particles which make up the sinter each is oriented in one direction, respectively, in at least the surface of the sinter. The entire sinte can be oriented.

Brief Summary Text (18):
Such an oriented sinter of a calcium phosphate type compound can be produced by a process comprising mixing an organic binder and wate an organic solvent with a powdered calcium phosphate type compound comprising rod-shaped crystal grains extending in the direction of on crystallographic axis, kneading the mixed components, extruding the resulting clay-like composition in a specified direction to shape the composition, thermally decomposing the organic binder, and firing the shaped article at a temperature of from 900.degree. to 1,400.degree. C

Detailed Description Text (2):
Examples of the calcium phosphate type compound of the present invention include hydroxyapatite, fluoroapatite, chloroapatite and tricalciu phosphate.

Detailed Description Text (3):
A commonly employed method for orienting grains in the direction of a certain crystallographic axis is by utilizing the electric or magnetic polarity of the grains. This method, however, is not highly effective in orienting the crystals of calcium phosphate type compounds because t polarity is rather low.

Detailed Description Text (4):
If calcium phosphate type compounds are synthesized by a wet method under properly selected conditions, it is possible to prepare rod-like crystal grains that are elongate in the direction of the c-axis as described in J. Am. Chem. Soc., Oct. 25, 1967, pp. 5535-5541. For instance, s grains can be synthesized by mixing a calcium compound with a phosphoric acid compound, the pH of the reaction solution being adjusted t either neutral or alkaline with the temperature held in the range of from 10.degree. to 100.degree. C. The ratio of the long axis to the short ax of the rod-like grains is preferably 1.1 or more, more preferably 1.5 or more, and particularly preferably 2.0 or more.

Detailed Description Text (7):
The secondary particles of a calcium phosphate type compound can be pulverized into primary particles when they are mixed with an organi binder and water or an organic solvent. If the slurry is not dried but is subjected to filtration, no secondary particles will form and the synthesized crystal grains may be directly used without being pulverized.

Detailed Description Text (8):
Therefore, in accordance with the present invention, the rod-shaped crystal grains of a calcium phosphate type compound are used as a starti powder, which is mixed with suitable amounts of a heat-decomposable organic binder and water or an organic solvent, as well as optionally with other additives such as a dispersant and a plasticizer. The ingredients are kneaded and the resulting clay-like composition is extruded to shape the same.

Detailed Description Text (16):
A slurry of hydroxyapatite synthesized by a conventional wet method (as described in J. Am. Chem. Soc., Oct. 25, 1967, pp. 5535-5541) wa spray-dried to make a powder having an average particle size of about 7 .mu.m. Observation under a scanning electron microscope showed t the powder was composed of spherical secondary particles which were dense agglomerations of elongate primary grains having a width of fr

200 to 500 .ANG. and length of about 1,000 .ANG.. These particles were calcined at 700.degree. C. for 4 hours and pulverized with a supersonic mill (product of Nippon Pneumatic Co., Ltd.) to obtain a fine powder having an average particle size of about 1 .mu.m. This fine powder (feed powder) was used as a starting material for the next shaping step.

Detailed Description Text (19):
The "degree of orientation" of hydroxyapatite as defined below is shown in Table 1 for each sample. As one can see from Table 1, the sinter the shaped articles prepared in Example 1 had the c-axis of the primary particles oriented in the direction of extrusion. However, the pulveriz products of these sinters showed no appreciable orientation and the relative intensities of individual diffraction lines were in accord with the data of ASTM 24-33.

Detailed Description Text (20):
The "degree of orientation" of hydroxyapatite as used herein is defined by ##EQU1## wherein I.sub.(300) is the diffraction intensity from th (300) face of a sample, and I.sub.(002) is the diffraction intensity from the (002) face of the sample. The ASTM value for I.sub.(300) /I.sub.(002) is 1.5.

Detailed Description Text (27):
A slurry containing 4% hydroxyapatite particles (based on total slurry weight) with a width of from 200 to 500 and a length of about 1,000 .ANG. was obtained by a conventional wet method of synthesis (as described in J. Am. Chem. Soc., Oct. 25, 1967, pp. 5535-5541). The slur was concentrated by filtration, and the following composition was obtained.

Detailed Description Text (28):
The composition containing the thus synthesized rod-shaped crystals of hydroxyapatite, a binder and water was spun by extrusion through an nozzle (diameter: 0.3 mm) at an air pressure of 900 mmH.sub.2 O according to JP-A-61-106166, and dried with hot air at 300.degree. C. to form a gauze-like shaped article. The dried article was sintered at 1,100.degree. C. for 4 hours and subjected to X-ray diffractiometry to chec for the occurrence of orientation. When an unpulverized sample of the gauze-like article was loaded in a glass sample holder, grain orientatio was observed in the same manner as in Examples 1 and 2.

Detailed Description Text (35):
An hydroxyapatite cylinderical molded article, which was molded, dried and degreased in the same manner as in Example 1, was fired at 1,100.degree. C. to obtain a sinter. The sinter was cut in the direction parallel to the molding direction or in the direction perpendicular to th molding direction. The cut surfaces were polished and measured for X-ray diffraction scans. The X-ray diffraction scan for the cut surface parallel to the molding direction is shown in FIG. 7. The X-ray diffraction scan for the cut surface perpendicular to the molding direction is shown in FIG. 8. Separately, the sinter was pulverized in a mortar and measured for an X-ray diffraction scan which is shown in FIG. 9.

Detailed Description Text (39):
An hydroxyapatite plate-like molded article, which was molded, dried and degreased in the same manner as in Example 4, was fired at 1,100.degree. C. to obtain a sinter. From the measurement of X-ray diffraction scans, it was found that the sinter had the same orientation properties as in the sinter obtained in Example 4.

Detailed Description Text (52):
In accordance with the present invention, a certain crystallographic axis of the primary particles in at least the surface or the entire portion of shaped article to be produced can be oriented in one direction by a simple method. The shaped article of a calcium phosphate calcium compound or the sinter thereof which is produced by the present invention has grain orientation so that their mechanical, electrical and chem properties are sufficiently anisotropic to provide improved characteristics over conventional materials. Further, the shaped article and sinter thereof are improved in fracture toughness.

Detailed Description Paragraph Table (2):

Composition	Amount
Hydroxyapatite	40%
Water	50%
Pullulan	10%

CLAIMS:

1. A process for producing an oriented shaped article of a calcium phosphate compound, which process comprises: mixing an organic binder and water or an organic solvent with a powder of a calcium phosphate compound comprising rod-shaped crystal grains extending in the direction of one crystallographic axis thereof, kneading the mixed components, and extruding the resulting composition in a specified directi to shape said composition.

4. The process of claim 1, wherein the calcium phosphate compound is hydroxyapatite.

7. The process of claim 1, wherein the composition which is extruded comprises hydroxyapatite, water, butyl alcohol, methyl cellulose, a wa emulsion and a stearic acid emulsion.

8. The process of claim 1, wherein the composition which is extruded comprises hydroxyapatite, butyl methacrylate, an ethylene-vinyl acetat copolymer, a wax emulsion, dibutyl phthalate and stearic acid.

9. A process for producing an oriented sinter of a calcium phosphate compound, which process comprises: mixing an organic binder and wa or an organic solvent with powder of the calcium phosphate compound comprising rod-shaped crystal grains extending in the direction of on crystallographic axis thereof, kneading the mixed components, extruding the resulting composition in a specified direction to shape said composition, thermally decomposing the organic binder, and firing the shaped article at a temperature of from 900.degree. to 1,400.degree. C

12. The process of claim 9, wherein the calcium phosphate compound is hydroxyapatite.

15. The process of claim 9, wherein the composition which is extruded comprises hydroxyapatite, water, butyl alcohol, methyl cellulose, a w emulsion and a stearic acid emulsion.

16. The process of claim 9, wherein the composition which is extruded comprises hydroxyapatite, butyl methacrylate, an ethylene-vinyl acet copolymer, a wax emulsion, dibutyl phthalate and stearic acid.

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L4: Entry 19 of 32 File: USPT

US-PAT-NO: 5336642
DOCUMENT-IDENTIFIER: US 5336642 A

TITLE: Canasite-apatite glass-ceramics

DATE-ISSUED: August 9, 1994

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Wolcott; Christine C.	Horseheads	NY		

US-CL-CURRENT: 501/3; 501/10, 501/57

CLAIMS:

I claim:

1. A glass-ceramic biomaterial having a bending strength greater than 25,000 psi (172 MPa), a fracture toughness greater than 2.3 Kpsi.times.in.sup.1/2 (2.5 MPa m.sup.1/2), a primary crystal phas of F-canasite, a secondary crystal phase of F-apatite, a crystal phase structure including interlocking blades of F-canasite with at least a portion of the F-apatite crystals within the interlocking F-canasite blades, and a residual glassy phase.

2. An SiO.sub.2 --CaO--Na.sub.2 O--K.sub.2 O--P.sub.2 O.sub.5 --F glass capable of being thermally converted to a glass-ceramic having F-canasite as a primary crystal phase and F-apatite as a secondary crystal phase and having a composition, as calculated i weight % on an oxide basis, consisting essentially of 42-70% SiO.sub.2, 20-30% CaO, 6-12% Na.sub.2 O, 3-10% K.sub.2 O, 2-13% P.sub.2 O.sub.5, and 3-11%.

3. A glass in accordance with claim 2 wherein the glass, as melted, is a clear glass containing no more than about 8 weight % P.sub.2 O.sub.5.

4. A glass in accordance with claim 2 wherein the glass, as melted, is an opal glass containing no more than about 8 weight % P.sub.2 O.sub.5.

5. A glass in accordance with claim 2 wherein the glass, as

melted, contains F-apatite crystals and 8-13 weight % P.sub.2 O.sub.5.

6. A glass in accordance with claim 2 wherein the glass is self nucleated by CaF.sub.2, P.sub.2 O.sub.5, or both.

7. A method of producing a glass-ceramic biomaterial having a primary crystal phase of F-canasite, and a secondary crystal phas of F-apatite, which comprises melting a glass having a composition, as calculated in weight % on an oxide basis, consisting, essentially of 42-70% SiO.sub.2, 20-30% CaO, 6-12% Na.sub.2 O, 3-10% K.sub.2 O, 2-13% P.sub.2 O.sub.5, and 3-11% F, cooling the glass below its transformation range and subjecting the glass to a treat treatment at a temperature higher than the glass transformation temperature range, but, not over 950.degree. C., for a time sufficient to produce F-canasite and F-apatite crystal phases.

8. A method in accordance with claim 7 wherein the heat treatment is in the temperature range of 685.degree.-950.degree. C. for a period of time ranging from four hours to one-half hour.

9. A method in accordance with claim 9 wherein the heat treatment is at a temperature of about 850.degree. C. for about one hour.

10. A method in accordance with claim 7 wherein the heat treatmen comprises an initial nucleation stage followed by a crystallization stage at a higher temperature.

11. A method in accordance with claim 10 wherein the initial nucleation stage is at a temperature in the range of 585.degree.-635.degree. C. and the crystallization is at a temperature in the range of 750.degree.-950.degree. C.

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L4: Entry 17 of 32

File: USPT

US-PAT-NO: 5652056
DOCUMENT-IDENTIFIER: US 5652056 A

TITLE: Hydroxyapatite filament

DATE-ISSUED: July 29, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Pepin; John N.	Greenville	ME	04441	

US-CL-CURRENT: 428/364; 423/308, 423/309, 423/311, 428/372

CLAIMS:

I claim:

1. A hydroxyapatite filament comprised of a mixture of hydroxyapatite and hydroxyapatite whiskers.

2. The hydroxyapatite filament of claim 1 having a tensile strength greater than 140 MPa.

3. The hydroxyapatite filament of claim 1 having a tensile modulu greater than 40 GPa.

4. The hydroxyapatite filament of claim 1 whose largest lateral dimension is greater than 5 microns and whose length is greater than 1 millimeter.

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L4: Entry 17 of 32 File: USPT

DOCUMENT-IDENTIFIER: US 5652056 A
TITLE: Hydroxyapatite filament

Abstract Text (1):
A substantially pure hydroxyapatite filament provides the reinforcement for composite materials used for bone replacement and repair. Its biocompatibility and high strength reveal opportunities for strong, tough and biocompatible composites to replace diseased, fractured or mis areas of bone. One such opportunity is a hydroxyapatite fiber reinforced hydroxyapatite matrix composite. This composite has higher strengt and toughness than sintered hydroxyapatite yet has excellent biocompatibilty and mechanical properties which can be tailored to mimic repla bone. Methods for filament fabrication include low temperature extrusion of a precursor gel filament reinforced with hydroxyapatite whisker high temperature sinter-extrusion and high temperature glass filament formation followed by reconversion to hydroxyapatite by intermediate temperature heat treatment.

Brief Summary Text (5):
Calcium phosphate based materials such as hydroxyapatite and .alpha. and .beta. tricalcium phosphate have been used as bone replacement materials in dental and orthopedic applications. These materials are completely biocompatible. Their bioresorbability or the rate at which the degrade and become absorbed when implanted into the body is dependent on constituent composition, crystal structure and porosity. The mineral content of bones and teeth is primarily hydroxyapatite. Hydroxyapatite is a crystalline material with the chemical formula Ca.sub.10 (PO.sub.4).sub.6 (OH).sub.2 having the Ca/P molar ratio of 1.67. Living host bone will form chemical bonds to hydroxyapatite so it has received a great deal of attention for bone replacement applications. Its synthetic form is often used to fill defects or build bone areas by allowing bone ingrowth into implanted hydroxyapatite particles and slurries. In dental applications it has been used to build up the alveolar ridge and fill areas of non-structural missing bone. Hydroxyapatite sintered from a microcrystalline powder has been used for small implants with low mechanical loading such as small bone implants for the ear. In still another application, plasma sprayed hydroxyapatite is used to co titanium hip implants for better fixation at their interface with the femur. Thus far, however, sintered hydroxyapatite has not been used for hi load bearing applications with complex stress states such as joint replacement prostheses because its current forms do not have the necessary strength and toughness to support high cyclic loads especially in tension and shear. It is also brittle and hence its strength is sensitive to inter and surface flaws.

Brief Summary Text (6):
In bone replacement applications where high strength and toughness is required, metals or combinations of metals, ceramics, and high densit plastics are used. Joint replacement prostheses, for example, are fabricated from cobalt chrome alloys, titanium, stainless steel, monolithic ceramics or other relatively inert material. While they initially have sufficient strength, these materials have moduli or stiffnesses which are a order of magnitude higher than the bone they are replacing. They are also mechanically isotropic, that is, they have the same properties in all directions within the material. Bone is a low modulus, anisotropic composite material whose reinforcement is tailored to support the loads it experiences. When bone is replaced with these high modulus materials the interfacing host bone tissues are shielded from experiencing natur occurring stress distributions. This stress shielding causes living bone tissue to resorb or become weaker and less dense. This further complicates fixation of the implant for long periods.

Brief Summary Text (8):
Several U.S. patents describe applications of hydroxyapatite, mainly as a coating material for strong substrate materials. Coating methods ar described in U.S. Pat. Nos. 5,279,831, 5,188,670, 5,128,169, and others. The incentive to use hydroxyapatite coatings is that the hydroxyapa enhances the growth of dense bone in its neighborhood and further that it bonds chemically to this new bone tissue. Coating a structural mate with hydroxyapatite takes advantage of these positive characteristics even though the hydroxyapatite itself, in prior art forms, does not have strength or toughness to be used as the load bearing structure of an implant. Coatings, however, are typically very thin interfaces which are subject to flaking, chipping and the like. In addition, they only provide a two-dimensional interface upon which bone can attach limiting the strength and toughness of this attachment.

Brief Summary Text (9):
Tagai, et al in U.S. Pat. Nos. 4,735,857 and 4,820,573 describe a calcium phosphate glass fiber with a Ca/P molar ratio between 0.2 and 0.6 The use of this fiber in a cotton-like staple form or cloth form is described as a bone defect filler to encourage bone growth into the defect;

however, the patents do not reveal the fiber's tensile strength or rate of resorption after implantation. A similar cotton-like product is describ by Fuji in U.S. Pat. No. 4,659,617. These fiber forms may be useful in bone filling applications but in many cases the removal of diseased bo or repair of broken bones requires fixation with structures which are strong, tough and completely biocompatible. Unlike pure crystalline hydroxyapatite which has been shown to be totally biocompatible, these prior art glass fibers are comprised of mixtures of several different materials at least in part to aid in processing into fiber. These mixtures will have varying biocompatibility, resorption, and strength and henc their application to long term bone replacement components supporting high mechanical loads will be limited.

Brief Summary Text (11):
It is the object of this invention to provide a high strength hydroxyapatite filament as a mechanical building block for a class of strong, tough biomaterials. More particularly, the objects and advantages of the present invention are:

Brief Summary Text (12):
(a) to provide strong hydroxyapatite filaments to reinforce a hydroxyapatite matrix material resulting in a composite material which displays excellent biocompatibility and durability when implanted as a bone replacement component or prosthesis. The mechanical properties of this composite material can be tailored to mimic the mechanical properties of the replaced bone thereby eliminating the stress shielding which occurs with currently used high modulus materials. This composite will also exhibit the necessary toughness and strength to support high mechanical loads in the area of the replaced bone. When implanted, sintered hydroxyapatite has a very high ability to enhance formation of dense, new bone around it and it has a very low rate of resorption. Unlike prior art materials, the hydroxyapatite fiber reinforced hydroxyapa matrix composite will be stable for long periods of time when implanted and, if wear particles are released from this composite, they will no cause the inflammatory response of the metals, ceramics and plastics currently used. The active fiber interface between this composite and th living bone tissue can be woven such that voids between filament bundles allow bone ingrowth to provide life-long fixation of an implant. Mechanically and biologically, this composite will be as close to living bone tissue as possible.

Brief Summary Text (13):
(b) to provide strong hydroxyapatite filaments in woven two-dimensional, three-dimensional, and multi-dimensional reinforced shapes which act as scaffolds for bone ingrowth while preserving needed strength during the bone growth process. A specific application for a hydroxyapa fabric would be a dam to prevent the growth of epithelial cells into a hydroxyapatite slurry injected below the gum line to build up the bone structures supporting teeth. The current practice uses a rubber dam to block epithelial cell growth into the implanted slurry to give bone the t to grow into the slurry. This rubber dam has to be removed surgically whereas a hydroxyapatite fabric dam could remain in place. The hydroxyapatite fabric dam would therefore eliminate this additional surgery with its cost, lost time and discomfort to the patient.

Brief Summary Text (14):
(c) to provide significant improvements in fixation of current metal implants by weaving hydroxyapatite filaments into the metal implant sur yielding a strong, three-dimensional interface for bone ingrowth. This three-dimensional interface will be formed by hydroxyapatite filament loops extending outward from the metal surface. Prior art methods use a hydroxyapatite coating which can break off, chip or flake reducing bone-implant interface strength and causing loosening of the implant.

Brief Summary Text (15):
It is a further object of the invention to provide a hydroxyapatite fiber reinforced composite material whose matrix is designed to resorb in a controlled manner. This will allow living tissue to grow into the implant to anchor it or perhaps eventually completely replace the matrix of a fiber reinforced composite implant. The living bone tissue is then capable of growth and remodeling to suit changing mechanical and physiological conditions. A gradient in the rate of resorption and hence rate of living bone intrusion into the matrix might also be provided b using several matrix materials having different rates of resorption. These materials could be deposited in layers from the inside of the implan composite to its outer, bone-interface surface.

Drawing Description Text (4):
FIG. 3 shows hydroxyapatite whiskers.

Drawing Description Text (5):
FIG. 4 shows a piston and cylinder extruding a gel containing hydroxyapatite into a dilute acid bath to form a precursor fiber.

Drawing Description Text (6):
FIG. 5 shows a furnace and die arrangement extruding a hydroxyapatite filament at high temperature.

Detailed Description Text (2):
In summary, bone replacement materials currently being used to replace highly loaded areas of bone like joint replacements are not well suit for this task because of their high stiffness and lack of complete biocompatibility. This invention starts with the most biocompatible material available, hydroxyapatite, and provides a strong form of this material, a filament. This filament can then be used to build an entire set of bon replacement materials and structures. These materials and structures will provide lifetime bone replacement components used in dental, maxillofacial and orthopedic reconstruction.

Detailed Description Text (4):
The invention is a hydroxyapatite filament and applications of the filament useful in bone replacement and repair. One such useful form is shown in FIG. 1. FIG. 1 shows a schematic of a cylinder 1 which is comprised of interwoven axial 2, radial 3, and circumferential 4 fiber bundles. Typical inside diameter 8, outside diameter 6 and length 10 dimensions are given in millimeters. Diameter dimensions are typical o those which might be required in replacing a section of long, highly loaded area of bone. In another embodiment, orientation of fiber bundle can be changed to suit a particular loading requirement of a bone section to be replaced. For example, to give cylinder 1 higher torsional stiffness, fiber bundles 2 currently shown in the axial direction could be oriented at an angle relative to the cylinder axis. The technology exi to weave these orthogonally reinforced cylinders. FIG. 2 shows a silica fiber reinforced silica matrix cylinder 12 whose dimensions approxim the values given for cylinder 1. The preform or woven fiber network of this cylinder can be obtained from Techniweave, Inc. in Rochester, N.H., U.S.A.

Detailed Description Text (5):
The technology to weave such a cylinder was developed by the aerospace industry. Multidirectionally woven filament bundles, or preforms, the reinforcing skeletons for silica fiber reinforced silica antenna windows and carbon fiber reinforced carbon missile nosetips and rocket nozzles. These combinations of fiber and matrix are instructive since high strength fibers combine with brittle matrices to yield composites which are strong, tough, and damage tolerant. For example, a steel nail can be hammered through a multidirectionally reinforced carbon-carb composite--a composite material with a brittle fiber reinforcing a brittle matrix. This characteristic is due to the network of microcracks in th composite allowing multiple failure paths and local yielding of the composite material in the area of high stresses. The aerospace industry is clearly distinct from the field of the invention and the constituent fibers and matrices of these aerospace composites do not have the biocompatibility and bone growth enhancing features of hydroxyapatite. However, if combined with a strong hydroxyapatite filament, the multidirectional weaving technology could be useful to fabricate woven shapes whose mechanical properties mimic those of replaced bone. Bone itself is a composite material with complex reinforcement orientations within it and the better the mechanical property simulation of replaced bone tissue, the better a bone replacement implant will perform.

Detailed Description Text (6):
Three-dimensional woven shapes, two-dimensional woven fabrics, chopped fiber mats, and random fiber felts are all examples of fiber form which can be combined with a matrix to yield a composite material for bone replacement and repair. One combination of constituent fiber an matrix which would result in an excellent bone replacement material is hydroxyapatite fiber reinforced hydroxyapatite. Such a composite wi strong hydroxyapatite fiber reinforcing a brittle hydroxyapatite matrix would yield a strong, tough, biocompatible, and mechanically tailorab bone replacement material. The hydroxyapatite filament reinforcement of these composites could be random or oriented and the composite could have either continuous or discontinuous hydroxyapatite filaments. Another embodiment would use the same hydroxyapatite fiber but a different matrix such as tricalcium phosphate, collagen, or polymerizable proteins. These would have controlled resorption so that living hos bone would grow into the fiber shape as the matrix resorbs and recedes from the bone/implant interface.

Detailed Description Text (7):
Unimpregnated preforms or free standing continuous filament woven shapes without any matrix have sufficient strength and post-weaving formability to be useful as a scaffold for bone ingrowth. Unlike the prior art cotton-like bone filling fibers, however, these preforms would provide significant mechanical integrity to a weakened area before and during the bone ingrowth and healing process. Bundles of hydroxyapatite filaments woven into these three-dimensional shapes would provide excellent biocompatibility, controlled porosity and mechanical strength. Bundle sizes in the woven shape could be in the range of 3000 to 12000 hydroxyapatite filaments.

Detailed Description Text (8):
What is needed to take advantage of this composite technology for bone replacement applications is a strong hydroxyapatite filament to prov the reinforcement. Filament diameters useful for the reinforcing applications mentioned are between 5 and 100 microns. A tensile strength in excess of 140 MPa would be useful but preferably the tensile strength should be above 300 MPa. The modulus of the fiber need not be high since bone itself has a rather low modulus. A modulus range of 40-500 GPa would be acceptable with the preferable range of 80-200 GPa.

Detailed Description Text (9):
Three methods are given for fabricating such a hydroxyapatite filament.

Detailed Description Text (11):
The first method uses hydroxyapatite whiskers 14 shown in FIG. 3. Whiskers of other materials such as silicon carbide are routinely used to reinforce ceramics, metals, and plastics due to their high strength. Hydroxyapatite whiskers are needle-like crystals of hydroxyapatite. They typically 8-20 microns long and the largest lateral dimension is less than 1 micron. Whiskers 14 are precipitated and grow like flowers in a solution. The hydroxyapatite whiskers are used to reinforce a hydroxyapatite filament along the axis of the filament giving the filament preferential strength along its axis.

Detailed Description Text (18):
There are occupational health issues associated with the manufacture and handling of whiskers if they become airborne. Hydroxyapatite whiskers should either be in a fluid medium or encapsulated in a matrix at all times. Once encapsulated the whiskers pose no problem even i the composite is machined. Resulting dust particles do not have the whisker shape and are handled in routine ways. Silicon carbide whiskers

similar in size to hydroxyapatite whiskers and guidelines for handling these are given in ASTM E 1437-91.

Detailed Description Text (21):
The hydroxyapatite filament is formed by drying the gel fiber for 24 hrs at room temperature and then heat treating it in air at 1100.degree.-1200.degree. C. for three hours. The ammonium alginate gel oxidizes completely leaving no ash residue in the hydroxyapatite filament.

Detailed Description Text (22):
In another embodiment of this method the whiskers are mixed with a microcrystalline hydroxyapatite powder before the ammonium alginate added. The powder eventually acts to bind the whiskers together in the filament. The volume fraction of whiskers-to-powder can range from volume percent to 60 volume percent. When whiskers and powder are mixed, the powder particle diameter must be smaller than the typical whisker cross section. Otherwise, the process is like trying to mix pencils with basketballs. A small powder particle size prevents separation the powder from the whiskers during mixing and ensures high density packing of whiskers within the powder. Also, it will allow the laminar flow of the fluid medium to orient the whiskers more easily during extrusion of the alginate mixture. Most of the particles of a sinterable hydroxyapatite powder are less than 60 microns in size. These particles are made up of loosely agglomerated microcrystals about 0.01 micro in size. When milled in deionized water these particles break up easily to form a colloidal suspension. The whiskers are mixed into this suspension with a ball mill or mixer. Finally, the ammonium alginate is added and mixed. A suitable microcrystalline hydroxyapatite powder available from CAM Implants in Leiden, The Netherlands.

Detailed Description Text (23):
The extrusion of this mixture is the same as discussed previously for forming the gel fiber with whiskers only. The process is shown in FIG. A mixture of water, ammonium alginate, hydroxyapatite whiskers, and hydroxyapatite powder 16 is placed in tube 22. Piston 24 pushes the mixture through a necked down region 20 in the glass tube. The ammonium alginate in the mixture gels as soon as it is exposed to acid 26. G fiber 18 is thus formed.

Detailed Description Text (24):
The gel fiber is then dried once again at room temperature for 24 hours and heated to the sintering temperature of hydroxyapatite--between 1100.degree. and 1200.degree. C. The hydroxyapatite whisker reinforced hydroxyapatite filament is formed as the ammonium alginate oxidi and the powder and whiskers sinter.

Detailed Description Text (27):
Method 2 is a high temperature sinter-extrusion process. The microcrystalline hydroxyapatite powder or powder/whisker mixture is heated to the sintering temperature of 1200.degree. C. and forced through an orifice to create the filament. FIG. 5 shows a schematic of this method. Powder mixture 34 is surrounded by die 32 which is supported by base 38. Furnace coils 30 contained within furnace boundary 36 heat the assembly to the desired temperature. At the sintering temperature a piston 28 pushes downward on the powder mixture forcing it through an orifice to form filament 40.

Detailed Description Text (28):
In a process called sinter-forging, known in the art, hydroxyapatite powder can be deformed under high pressure at its sintering temperature. High temperature extrusion of submicron diameter ceramic powders has also been done using area ratios of piston-to-extruded shape of 5 to High temperature extrusion is aided if the hydroxyapatite powder has submicron diameter particles and a small amount of additive such as a glass is used as a lubricant at the sintering temperature.

Detailed Description Text (30):
Method 3 forms the hydroxyapatite filament in much the same way glass filaments are formed commercially. The hydroxyapatite powder is heated to a temperature in excess of 1400.degree. C. until it forms a glass in a viscosity range which can be pulled through one or more orific and cooled. The furnace arrangement is similar to FIG. 5. The range of orifice sizes for this method is 0.5-3 mm in diameter. As the molten glass filament is pulled through each orifice it forms a meniscus or necks down to a diameter between the desired 5-100 microns. It is cooled rapidly, a coating or sizing is added to protect the filament surfaces and the filaments are then wound on a take up spool. This process is wel known in the art. At this point, however, the filament is no longer the crystalline hydroxyapatite, having lost its crystalline structure and its hydroxyl (OH) groups during the high temperature processing. The filament is a metaphosphate glass. This glass filament can then be reconverted to a hydroxyapatite filament by heat treating it in air at 600.degree. C. for 1 to 3 hours.

Detailed Description Text (31):
A variation of method 3 includes formation of the glass filament by means other than extrusion through a hole. These means include droppin the glass onto a spinning disk or blowing air into a molten glass pool to fiberize the glass. These methods, also known in the art, would prov the glass filament precursor to the hydroxyapatite filament.

Detailed Description Text (33):
Thus the hydroxyapatite filament of the current invention provides a biocompatible building block from which many materials for bone replacement and repair are possible. As a reinforcement fiber for composite bone replacement implants it provides the needed toughness and

strength. Due to its high temperature stability and inertness it can be processed with many matrix materials. These matrix materials may be stable in vivo, resorb in a controlled manner, provide timed release of medication, or provide other necessary functions. Bundles, yards or to of hydroxyapatite filaments woven into two-dimensional, three dimensional, or multidimensional forms can provide a stable scaffold for bon ingrowth while retaining tailored mechanical properties while the ingrowth occurs.

Other Reference Publication (1):
Yoshimura et al, Processing and Mechanical Properties of Hydroxyapatite (HAP) reinforced with HAP Whiskers; 1996, pp. 1715-1723.

CLAIMS:

1. A hydroxyapatite filament comprised of a mixture of hydroxyapatite and hydroxyapatite whiskers.

2. The hydroxyapatite filament of claim 1 having a tensile strength greater than 140 MPa.

3. The hydroxyapatite filament of claim 1 having a tensile modulus greater than 40 GPa.

4. The hydroxyapatite filament of claim 1 whose largest lateral dimension is greater than 5 microns and whose length is greater than 1 millimeter.

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L4: Entry 17 of 32 File: USPT Jul 29, 1997

US-PAT-NO: 5652056
DOCUMENT-IDENTIFIER: US 5652056 A

TITLE: Hydroxyapatite filament

DATE-ISSUED: July 29, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Pepin; John N.	Greenville	ME	04441	

APPL-NO: 08/ 709440 [PALM]
DATE FILED: August 20, 1996

INT-CL: [06] D02 G 3/00, C01 B 15/16

US-CL-ISSUED: 428/364; 428/372, 423/308, 423/309, 423/311
US-CL-CURRENT: 428/364; 423/308, 423/309, 423/311, 428/372

FIELD-OF-SEARCH: 428/364, 428/372, 423/308, 423/309, 423/311, 501/95, 206/35

PRIOR-ART-DISCLOSED:

U.S. PATENT DOCUMENTS

Search Selected | Search ALL

PAT-NO	ISSUE-DATE	PATENTEE-NAME	US-CL
4503157	March 1985	Hatahira	423/308
4880610	November 1989	Constantz	423/309
4968317	November 1990	Tormala et al.	606/77
5227147	July 1993	Yoshimura et al.	428/311

OTHER PUBLICATIONS

Yoshimura et al, Processing and Mechanical Properties of Hydroxyapatite (HAP) reinforced with HAP Whiskers; 1996, pp. 1715-1723.

ART-UNIT: 137

PRIMARY-EXAMINER: Edwards; Newton

ABSTRACT:

A substantially pure hydroxyapatite filament provides the reinforcement for composite materials used for bone replacement and repair. Its biocompatibility and high strength reveal opportunities for strong, tough and biocompatible composites to replace diseased, fractured or mis areas of bone. One such opportunity is a hydroxyapatite fiber reinforced hydroxyapatite matrix composite. This composite has higher strengt

and toughness than sintered hydroxyapatite yet has excellent biocompatibilty and mechanical properties which can be tailored to mimic repla bone. Methods for filament fabrication include low temperature extrusion of a precursor gel filament reinforced with hydroxyapatite whisker high temperature sinter-extrusion and high temperature glass filament formation followed by reconversion to hydroxyapatite by intermediate temperature heat treatment.

4 Claims, 5 Drawing figures

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L4: Entry 13 of 32 File: USPT

US-PAT-NO: 6017390
DOCUMENT-IDENTIFIER: US 6017390 A

TITLE: Growth of oriented crystals at polymerized membranes

DATE-ISSUED: January 25, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Charych; Deborah H.	Albany	CA		
Berman; Amir	Ben-Shiva			IL

US-CL-CURRENT: 117/68; 117/72, 117/925, 117/926, 117/927, 117/937, 117/938, 117/944, 428/323, 428/451, 428/689, 428/700

CLAIMS:

We claim:

1. A method for growing aligned crystals at a polymerized film comprising the steps of:

a) providing:

i) diacetylene self-assembling monomers;

ii) a formation support;

iii) a polymerization means; and

iii) a mineral source;

b) exposing said diacetylene self-assembling monomers to said formation support to produce a film;

c) polymerizing said film with said polymerization means to produce a template film; and

d) introducing said mineral source to said template film to form said aligned crystals.

2. The method of claim 1, wherein said diacetylene self-assemblin monomers are selected from the group consisting of

10,12-pentacosadiynoic acid, 5,7-pentacosadiynoic acid, sulfate-derivatized 10,12-pentacosadiynoic acid, sulfate-derivatized 5,7-pentacosadiynoic acid, and combinations thereof.

3. The method of claim 2, wherein said self-assembling monomers contain head groups selected from the group consisting of --COOH, --CH.sub.2 OH, --CH.sub.2 OCONHPh, --CH.sub.2 OCONEt, --CH.sub.2 CH(Et)OCONHPh, --(CH.sub.2).sub.9 OH, --CH.sub.2 OCOPh, --CH.sub. OCHONHMe, --CH.sub.2 OTs, --CH(OH)Me, --CH.sub.2 OCOR.sub.2, wherein R.sub.2 is n-CH.sub.5 H.sub.11, n-C.sub.7 H.sub.15, n-C.sub.9 H.sub.19, n-C.sub.11 H.sub.23, n-C.sub.13 H.sub.27, n-C.sub.15 H.sub.31, n-C.sub.17 H.sub.35, Ph, PhO, or o-(HO.sub.2 C)C.sub.6 H.sub.4, --OSO.sub.2 R.sub.2, wherein R.sub.2 is Ph, p-MeC.sub.6 H.sub.4, p-FC.sub.6 H.sub.4, p-CIC.sub.6 H.sub.4, pBrC.sub.6 H.sub.4, p-MeOC.sub.6 H.sub.4, m-CF.sub.3 C.sub.6 H.sub.4, 2-C.sub.10 H7, or Me--CO.sub.2 M, wherein M is K, H, or a/2, --CH.sub.2 OCONHR.sub.2 or --CH.sub.2 CONHR.sub.2 where R.sub.2 is Et, n-Bu, n-C.sub.6 H.sub.13, n-C.sub.8 H.sub.17, n-C.sub.12 H.sub.25, cyclo C.sub.6 H.sub.11, Ph, p-MeC.sub.6 H.sub.4, m-MeC.sub.6 H.sub.4, o-CIC.sub.6 H.sub.4, m-CIC.sub.6 H.sub.4, p-CIC.sub.6 H.sub.4, o-MeOC.sub.6 H.sub.4, 3-Thienyl, Me Et, Ph, 1-C.sub.10 H.sub.7, Et, Ph, EtOCOCH.sub.2, BuOCOCH.sub.2, Me, Et, i-Pr, n-C.sub.6 H.sub.13, EtOCOCH.sub.2, BuOCOCH.sub.2, Ph, 2,4(NO.sub.2).sub.2 C.sub.6 H.sub.3 OCH.sub.2, and CH.sub.2 CH.sub.2 OH.

4. The method of claim 1, wherein said mineral source comprises a supersaturated solution of dissolved mineral.

5. The method of claim 4, wherein said dissolved mineral is solubilized in aqueous solution.

6. The method of claim 1, wherein said mineral source is selected from the group consisting of calcium carbonate, iron oxide, manganese oxide, cadmium sulfide, cadmium selenide, tin oxide, aluminum oxide, lead sulfide, titanium oxide, indium phosphate, calcium phosphate, hydroxy apatite, mercury sulfide, tungsten oxide, nanocrystalline gold, nanocrystalline silver, nanocrystalline platinum, carbon nanotubes, boron nanotubes, C.sub.60 buckeyballs, and C.sub.70 buckeyballs.

7. The method of claim 1, wherein said formation support comprise a Langmuir-Blodgett trough.

8. The method of claim 1, further comprising the steps of:

f) providing a solid support; and

g) transferring said template film to said solid support followin said polymerizing step but before introducing said mineral source

9. The method of claim 8, wherein said solid support comprises a hydrophobized, horizontal support.

10. The method of claim 1, wherein said film is compressed into a monolayer having a surface tension range of approximately twenty to forty millinewtons per meter prior to said polymerizing.

11. The method of claim 1, wherein said polymerization means is selected from the group consisting of UV-irradiation, gamma irradiation, X-ray irradiation, and electron beam exposure.

12. The method of claim 1, wherein said introducing said mineral source to said template film comprises placing an aliquot of said mineral source onto said template film.

13. The method of claim 1, further comprising providing a solvent and an etched film support.

14. The method of claim 13, wherein in said step c) said polymerizing produces an etched film, and further comprising steps:

h) washing said etched film with said solvent after said polymerizing but before said introduction of said mineral source; and

i) transferring said etched film to said etched film support afte said washing but before said introduction of said mineral source.

15. The method of claim 13, wherein said etched film support comprises a semiconducting or metallic substrate.

16. The method claim 15, wherein said semiconducting or metallic substrate is selected from the group consisting of gold, titanium oxide, and gallium arsenate.

17. Aligned crystals produced according to the methods of claim 13.

18. Aligned crystals produced according to the methods of claim 1

19. A method for growing totally aligned crystals on polymerized organic nanostructures comprising the steps of:

a) providing:

i) at least two compounds capable of forming a self-assembling monolayer;

ii) a solid support;

iii) a polymerization means;

iv) a template film;

v) a mineral source; and

vi) an energetic beam emitter;

b) placing said compounds on said solid support;

c) etching said film with said energetic beam emitter to produce an etched film;

d) disposing said template film on said etched film;

e) polymerizing said template film with said polymerization means and

f) introducing said mineral source to said template film to produce said totally aligned crystals.

20. The method of claim 19, wherein said template film comprises self-assembling monomers selected from the group consisting of diacetylenes, acetylenes, alkenes, thiophenes, imides, acrylamides, methacrylates, vinylether, malic anhydride, urethanes, allylamines, siloxanes anilines, pyrroles, vinylpyridinium.

21. The method of claim 20, wherein said diacetylenes are selecte from the group consisting of 10,12-pentacosadiynoic acid, 5,7-pentacosadiynoic acid, sulfate-derivatized 10,12-pentacosadiynoic acid, sulfate-derivatized 5,7-pentacosadiynoic acid, and combinations thereof.

22. The method of claim 20, wherein said self-assembling monomers

contain head groups selected from the group consisting of --COOH, --CH.sub.2 OH, --CH.sub.2 OCONHPh, --CH.sub.2 OCONEt, --CH.sub.2 CH(Et)OCONHPh, --CH.sub.2).sub.9 OH, --CH.sub.2 OCOPh, --CH.sub.2 OCHONHMe, --CH.sub.2 OTs, --CH(OH)Me, --CH.sub.2 OCOR.sub.2, wherein R.sub.2 is n-CH.sub.5 H.sub.11, n-C.sub.7 H.sub.15, n-C.sub.9 H.sub.19, n-C.sub.11 H.sub.23, n-C.sub.13 H.sub.27, n-C.sub.15 H.sub.31, n-C.sub.17 H.sub.35, Ph, PhO, or o-(HO.sub.2 C)C.sub.6 H.sub.4, --OSO.sub.2 R.sub.2, wherein R.sub.2 is Ph, P-MeC.sub.6 H.sub.4, p-FC.sub.6 H.sub.4, p-CIC.sub.6 H.sub.4, pBrC.sub.6 H.sub.4, p-MeOC.sub.6 H.sub.4, m-CF.sub.3 C.sub.6 H.sub.4, 2-C.sub.10 H7, or Me--CO.sub.2 M, wherein M is K, H, or a/2, --CH.sub.2 OCONHR.sub.2 or --CH.sub.2 CONHR.sub.2 where R.sub.2 is Et, n-Bu, n-C.sub.6 H.sub.13, n-C.sub.8 H.sub.17, n-C.sub.12 H.sub.25, cyclo C.sub.6 H.sub.11, Ph, p-MeC.sub.6 H.sub.4, m-MeC.sub.6 H.sub.4, o-CIC.sub.6 H.sub.4, m-CIC.sub.6 H.sub.4, p-CIC.sub.6 H.sub.4, o-MeOC.sub.6 H.sub.4, 3-Thienyl, Me Et, Ph, 1-C.sub.10 H.sub.7, Et, Ph, EtOCOCH.sub.2, BuOCOCH.sub.2, Me, Et, i-Pr, n-C.sub.6 H.sub.13, EtOCOCH.sub.2, BuOCOCH.sub.2, Ph, 2,4(NO.sub.2).sub.2 C.sub.6 H.sub.3 OCH.sub.2, or CH.sub.2 CH.sub.2 OH.

23. The method of claim 19, wherein said mineral source comprises a supersaturated solution of dissolved mineral.

24. The method of claim 19, wherein said dissolved mineral is solubilized in aqueous solution.

25. The method of claim 19, wherein said mineral source is selected from the group consisting of calcium carbonate, iron oxide, manganese oxide, cadmium sulfide, cadmium selenide, tin oxide, aluminum oxide, lead sulfide, titanium oxide, indium phosphate, calcium phosphate, hydroxy apatite, mercury sulfide, tungsten oxide, nanocrystalline gold, nanocrystalline silver, nanocrystalline platinum, carbon nanotubes, boron nanotubes, C.sub.60 buckeybalss, and C.sub.70 buckeyballs.

26. The method of claim 19, wherein said polymerization means is selected from the group consisting of UV-irradiation, gamma irradiation, X-ray irradiation, and electron beam exposure.

27. The method of claim 19, wherein said introducing said mineral source to said template film comprises placing an aliquot of said mineral source onto said template film.

28. The method of claim 19, wherein said solid support comprises semiconducting or metallic substrate.

29. The method of claim 28, wherein said semiconducting or metallic substrate is selected from a group consisting of gold, titanium oxide, and gallium arsenate.

30. The method of claim 19, wherein said energetic beam emitter emits beams selected from the group consisting of ion beams and electron beams.

31. The method of claim 19, wherein said film is compressed prior to said etching.

32. Aligned crystals produced according to the methods of claim 18.

33. A composition comprising totally aligned crystals on polymerized film.

34. The composition of claim 33, whereby said totally aligned crystals are selected from the group consisting of calcium carbonate, iron oxide, manganese oxide, cadmium sulfide, cadmium selenide, tin oxide, aluminum oxide, lead sulfide, titanium oxide indium phosphate, calcium phosphate, hydroxy apatite, mercury sulfide, tungsten oxide, nanocrystalline gold, nanocrystalline silver, nanocrystalline platinum, carbon nanotubes, boron nanotubes, C.sub.60 buckeyballs, and C.sub.70 buckeyballs.

35. A method for growing totally aligned crystals at a polymerize film comprising the steps of:

a) providing:

i) self-assembling monomers;

ii) a formation support;

iii) a polymerization means; and

iii) a mineral source;

b) exposing said self-assembling monomers to said formation support to produce a film;

c) polymerizing said film with said polymerization means to produce a template film;

d) introducing said mineral source to said template film to form said crystals.

36. The method of claim 35, wherein said self-assembling monomers are selected from the group consisting of diacetylenes, acetylenes, alkenes, thiophenes, imides, acrylamides, methacrylates, vinyether, malic anhydride, urethanes, allylamines siloxanes anilines, pyrroles, and vinylpyridinium.

37. The method of claim 36, wherein said diacetylenes are selecte from a group consisting of 10,12-pentacosadiynoic acid, 5,7-pentacosadiynoic acid, sulfate-derivatized 10,12-pentacosadiynoic acid, sulfate-derivatized 5,7-pentacosadiynoic acid, and combinations thereof.

38. The method of claim 35, wherein said mineral source is selected from the group consisting of calcium carbonate, iron oxide, manganese oxide, cadmium sulfide, cadmium selenide, tin oxide, aluminum oxide, lead sulfide, titanium oxide, indium phosphate, calcium phosphate, hydroxy apatite, mercury sulfide, tungsten oxide, nanocrystalline gold, nanocrystalline silver, nanocrystalline platinum, carbon nanotubes, boron nanotubes, C.sub.60 buckeyballs, and C.sub.70 buckeyballs.

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L2	l1 and agglomeration	879	L2
L1	(calcium phosphate or apatite or hydroxylapatite or hydroxyapatite or calcium fluoride or fluorapatite o0r amorphous calcium phosphate or fluorophosphate calcium or calcium fluorophosphate or fluorine-doped hydroxylapatite or f-doped hydroxylapatite)	47239	L1

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L2	11 and agglomeration	879	L2
L1	(calcium phosphate or apatite or hydroxylapatite or hydroxyapatite or calcium fluoride or fluorapatite o0r amorphous calcium phosphate or fluorophosphate calcium or calcium fluorophosphate or fluorine-doped hydroxylapatite or f-doped hydroxylapatite)	47239	L1

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L8	l3 and (toothpaste or dentifrice or stomatol? or teeth or dental)	48	L8
L7	l5 and l2	0	L7
L6	l5 and nano?.clm.	0	L6
L5	l1 and nano?	35	L5
L4	l3 and crystals and particle size	32	L4
L3	l1 and (anisometric or anisotropic)	307	L3
L2	l1 and agglomeration	879	L2
L1	(calcium phosphate or apatite or hydroxylapatite or hydroxyapatite or calcium fluoride or fluorapatite o0r amorphous calcium phosphate or fluorophosphate calcium or calcium fluorophosphate or fluorine-doped hydroxylapatite or f-doped hydroxylapatite)	47239	L1

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US-PAT-NO: 5240659
DOCUMENT-IDENTIFIER: US 5240659 A

TITLE: Process for producing shaped article of oriented calcium phosphate type compound

DATE-ISSUED: August 31, 1993

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
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Ogawa; Tetsuro	Tokyo			JP
Sumita; Masaya	Tokyo			JP
Yokoo; Akihiko	Tokyo			JP

US-CL-CURRENT: 264/639; 264/108, 264/109, 264/125, 264/645

CLAIMS:

What is claimed is:

1. A process for producing an oriented shaped article of a calciu phosphate compound, which process comprises: mixing an organic binder and water or an organic solvent with a powder of a calcium phosphate compound comprising rod-shaped crystal grains extending in the direction of one crystallographic axis thereof, kneading the mixed components, and extruding the resulting composition in specified direction to shape said composition.

2. The process of claim 1, wherein at least two crystallographic axes of primary particles of which said oriented shaped article i composed each is oriented in one direction, respectively, in at least the surface of said article.

3. The process of claim 2, wherein said at least two crystallographic axes of the primary particles of which said oriented shaped article is composed each is oriented in one direction, respectively, in the entire portion of said article.

4. The process of claim 1, wherein the calcium phosphate compound is hydroxyapatite.

5. The process of claim 1, where the extruding is extrusion

molding at a molding pressure of from 0.2 to 500 kg/cm.sup.2.

6. The process of claim 1, wherein the extruding is injection molding at a molding pressure of from 500 to 3,000 kg/cm.sup.2.

7. The process of claim 1, wherein the composition which is extruded comprises hydroxyapatite, water, butyl alcohol, methyl cellulose, a wax emulsion and a stearic acid emulsion.

8. The process of claim 1, wherein the composition which is extruded comprises hydroxyapatite, butyl methacrylate, an ethylene-vinyl acetate copolymer, a wax emulsion, dibutyl phthalate and stearic acid.

9. A process for producing an oriented sinter of a calcium phosphate compound, which process comprises: mixing an organic binder and water or an organic solvent with powder of the calcium phosphate compound comprising rod-shaped crystal grains extending in the direction of one crystallographic axis thereof, kneading the mixed components, extruding the resulting composition in a specified direction to shape said composition, thermally decomposing the organic binder, and firing the shaped article at temperature of from 900.degree. to 1,400.degree. C.

10. The process of claim 9, wherein at least two crystallographic axes of primary particles of which said oriented shaped sinter is composed each is oriented in one direction, respectively, in at least the surface of said sinter.

11. The process of claim 10, wherein said at least two crystallographic axes of the primary particles of which said oriented shaped sinter is composed each is oriented in one direction, respectively, in the entire portion of said sinter.

12. The process of claim 9, wherein the calcium phosphate compoun is hydroxyapatite.

13. The process of claim 9, where the extruding is extrusion molding at a molding pressure of from 0.2 to 500 kg/cm.sup.2.

14. The process of claim 9, wherein the extruding is injection molding at a molding pressure of rom 500 to 3,000 kg/cm.sup.2.

15. The process of claim 9, wherein the composition which is extruded comprises hydroxyapatite, water, butyl alcohol, methyl cellulose, a wax emulsion and a stearic acid emulsion.

16. The process of claim 9, wherein the composition which is extruded comprises hydroxyapatite, butyl methacrylate, an ethylene-vinyl acetate copolymer, a wax emulsion, dibutyl phthalate and stearic acid.

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DOCUMENT-IDENTIFIER: US 5240659 A
TITLE: Process for producing shaped article of oriented calcium phosphate type compound

Abstract Text (1):
An oriented shaped article of a calcium phosphate type compound is disclosed, in which at least two crystallographic axes of the primary particles of which the shaped article is composed each is oriented in one direction, respectively, in at least the surface of said article. A sinte the oriented shaped article and a processes for producing the article and the sinter are also disclosed.

Brief Summary Text (2):
The present invention relates to shaped articles of calcium phosphate type compounds useful as biomaterials (e.g., artificial teeth and bones) as materials for humidity sensors, filters or IC substrates. The present invention also relates to sinters of these shaped articles and processes f producing the shaped articles and the sinters.

Brief Summary Text (4):
Due to their high biocompatibility, calcium phosphate type ceramics have conventionally been used as biomaterials such as artificial tooth ro and bones. Because the crystal particles (primary particles) of these ceramics are unoriented and these ceramics are unoriented polycrystallin bodies, the mechanical properties of these ceramics are isotropic. When these ceramics are placed under stress, the propagation of a fracture will travel over the shortest distance irrespective of the direction in which the stress is applied and the surface energy for a fracture becomes small that it will eventually cause a reduction in the fracture toughness of a shaped article of these ceramics and hence sinters thereof. Attem have been made to increase the strength of these ceramics by sintering them for high density after performing a suitable treatment such as HI (hot isotactic press), but no success has been achieved in improving their fracture toughness (as described, e.g., in Preprints of Annual Meeti of the Ceramics Society of Japan 1984, 3G10, pp. 939, published on May 14, 1984).

Brief Summary Text (5):
Hydroxyapatite which is in the class of calcium phosphate type compounds has ionic conductivity and research has been undertaken to study use as an electronic material in devices such as humidity sensors. However, conventional hydroxyapatite ceramics are also isotropic with res to electrical properties, and conduction ions in the ceramics are diffused at grain boundaries, making it impossible to provide satisfactory conductivity to the ceramics (As described, e.g., in Preprints of 2nd Apatite Meeting, pp. 22, published on Dec. 1, 1986).

Brief Summary Text (6):
In order to exploit the above various properties of calcium phosphate type ceramics in an advantageous way, it is necessary that shaped artic or sinters thereof have anisotropy. The ideal method for meeting this need would be to use single crystals of these ceramics. However, it is generally difficult to prepare large single crystals of calcium phosphate, and, in fact, no report has been published that describes success in preparing large single crystals of calcium phosphate.

Brief Summary Text (7):
In order to attain anisotropy for various properties of shaped articles and sinters, it is nessesary that at least two crystallographic axes or at le two crystal faces each must be oriented in one direction, respectively. For example, in tubular bones of animals, the c axis of apatite crystals the bone is oriented in the direction parallel to the longitudinal direction of the bone, and the a axis thereof is oriented in the direction perpendicular to the longitudinal direction of the bone, by which the anisotropy of the mechanical properties is attained.

Brief Summary Text (8):
Hydroxyapatite sinters in which one crystal face of the crystalline particles is oriented by hot-pressing has been reported in Preprints of Annu Meeting of the Ceramic Society of Japan 1984, A-72, pp. 511, published on May 14, 1984. In this method, because tabular (platelike) crysta are used, the (h00) plane is oriented in the pressing direction, but there is no research whether other planes (such as the (001) plane) are orien in one direction. Therefore, it is unknown whether sinters having anisotropy for mechanical properties are obtained by this method.

Brief Summary Text (10):
The present inventors therefore conducted intensive studies in order to develop calcium phosphate type ceramics in which the crystal grains

(i.e., the primary particles) are oriented in one direction and thus succeeded in reaching the present invention.

Brief Summary Text (11):
One object of the present invention is to provide a shaped article of an oriented calcium phosphate type compound.

Brief Summary Text (12):
Another object of the present invention is to provide a sinter of a shaped article of an oriented calcium phosphate type compound.

Brief Summary Text (15):
The present invention provides a shaped article of a calcium phosphate type compound in which at least two crystallographic axes of the primary particles which make up the shaped article each is oriented in one direction, respectively, in at least the surface of the article. Such orientation can be throughout the entire article.

Brief Summary Text (16):
Such an oriented shaped article of a phosphate type compound can be produced by a process which comprises mixing an organic binder and water or an organic solvent with a powdered calcium phosphate type compound comprising rod-shaped crystal grains extending in the direct of one crystallographic axis thereof, kneading the mixed components, and extruding the resulting clay-like composition in a specified directi to shape the composition.

Brief Summary Text (17):
The present invention also provides an oriented sinter of a calcium phosphate type compound in which at least two crystallographic axes of t primary particles which make up the sinter each is oriented in one direction, respectively, in at least the surface of the sinter. The entire sinte can be oriented.

Brief Summary Text (18):
Such an oriented sinter of a calcium phosphate type compound can be produced by a process comprising mixing an organic binder and wate an organic solvent with a powdered calcium phosphate type compound comprising rod-shaped crystal grains extending in the direction of on crystallographic axis, kneading the mixed components, extruding the resulting clay-like composition in a specified direction to shape the composition, thermally decomposing the organic binder, and firing the shaped article at a temperature of from 900.degree. to 1,400.degree. C

Detailed Description Text (2):
Examples of the calcium phosphate type compound of the present invention include hydroxyapatite, fluoroapatite, chloroapatite and tricalciu phosphate.

Detailed Description Text (3):
A commonly employed method for orienting grains in the direction of a certain crystallographic axis is by utilizing the electric or magnetic polarity of the grains. This method, however, is not highly effective in orienting the crystals of calcium phosphate type compounds because t polarity is rather low.

Detailed Description Text (4):
If calcium phosphate type compounds are synthesized by a wet method under properly selected conditions, it is possible to prepare rod-like crystal grains that are elongate in the direction of the c-axis as described in J. Am. Chem. Soc., Oct. 25, 1967, pp. 5535-5541. For instance, s grains can be synthesized by mixing a calcium compound with a phosphoric acid compound, the pH of the reaction solution being adjusted t either neutral or alkaline with the temperature held in the range of from 10.degree. to 100.degree. C. The ratio of the long axis to the short ax of the rod-like grains is preferably 1.1 or more, more preferably 1.5 or more, and particularly preferably 2.0 or more.

Detailed Description Text (7):
The secondary particles of a calcium phosphate type compound can be pulverized into primary particles when they are mixed with an organi binder and water or an organic solvent. If the slurry is not dried but is subjected to filtration, no secondary particles will form and the synthesized crystal grains may be directly used without being pulverized.

Detailed Description Text (8):
Therefore, in accordance with the present invention, the rod-shaped crystal grains of a calcium phosphate type compound are used as a starti powder, which is mixed with suitable amounts of a heat-decomposable organic binder and water or an organic solvent, as well as optionally with other additives such as a dispersant and a plasticizer. The ingredients are kneaded and the resulting clay-like composition is extruded to shape the same.

Detailed Description Text (16):
A slurry of hydroxyapatite synthesized by a conventional wet method (as described in J. Am. Chem. Soc., Oct. 25, 1967, pp. 5535-5541) wa spray-dried to make a powder having an average particle size of about 7 .mu.m. Observation under a scanning electron microscope showed t the powder was composed of spherical secondary particles which were dense agglomerations of elongate primary grains having a width of fr

200 to 500 .ANG. and length of about 1,000 .ANG.. These particles were calcined at 700.degree. C. for 4 hours and pulverized with a supersonic mill (product of Nippon Pneumatic Co., Ltd.) to obtain a fine powder having an average particle size of about 1 .mu.m. This fine powder (feed powder) was used as a starting material for the next shaping step.

Detailed Description Text (19):
The "degree of orientation" of hydroxyapatite as defined below is shown in Table 1 for each sample. As one can see from Table 1, the sinter the shaped articles prepared in Example 1 had the c-axis of the primary particles oriented in the direction of extrusion. However, the pulveriz products of these sinters showed no appreciable orientation and the relative intensities of individual diffraction lines were in accord with the data of ASTM 24-33.

Detailed Description Text (20):
The "degree of orientation" of hydroxyapatite as used herein is defined by ##EQU1## wherein I.sub.(300) is the diffraction intensity from th (300) face of a sample, and I.sub.(002) is the diffraction intensity from the (002) face of the sample. The ASTM value for I.sub.(300) /I.sub.(002) is 1.5.

Detailed Description Text (27):
A slurry containing 4% hydroxyapatite particles (based on total slurry weight) with a width of from 200 to 500 and a length of about 1,000 .ANG. was obtained by a conventional wet method of synthesis (as described in J. Am. Chem. Soc., Oct. 25, 1967, pp. 5535-5541). The slur was concentrated by filtration, and the following composition was obtained.

Detailed Description Text (28):
The composition containing the thus synthesized rod-shaped crystals of hydroxyapatite, a binder and water was spun by extrusion through an nozzle (diameter: 0.3 mm) at an air pressure of 900 mmH.sub.2 O according to JP-A-61-106166, and dried with hot air at 300.degree. C. to form a gauze-like shaped article. The dried article was sintered at 1,100.degree. C. for 4 hours and subjected to X-ray diffractiometry to chec for the occurrence of orientation. When an unpulverized sample of the gauze-like article was loaded in a glass sample holder, grain orientatio was observed in the same manner as in Examples 1 and 2.

Detailed Description Text (35):
An hydroxyapatite cylinderical molded article, which was molded, dried and degreased in the same manner as in Example 1, was fired at 1,100.degree. C. to obtain a sinter. The sinter was cut in the direction parallel to the molding direction or in the direction perpendicular to th molding direction. The cut surfaces were polished and measured for X-ray diffraction scans. The X-ray diffraction scan for the cut surface parallel to the molding direction is shown in FIG. 7. The X-ray diffraction scan for the cut surface perpendicular to the molding direction is shown in FIG. 8. Separately, the sinter was pulverized in a mortar and measured for an X-ray diffraction scan which is shown in FIG. 9.

Detailed Description Text (39):
An hydroxyapatite plate-like molded article, which was molded, dried and degreased in the same manner as in Example 4, was fired at 1,100.degree. C. to obtain a sinter. From the measurement of X-ray diffraction scans, it was found that the sinter had the same orientation properties as in the sinter obtained in Example 4.

Detailed Description Text (52):
In accordance with the present invention, a certain crystallographic axis of the primary particles in at least the surface or the entire portion of shaped article to be produced can be oriented in one direction by a simple method. The shaped article of a calcium phosphate calcium compound or the sinter thereof which is produced by the present invention has grain orientation so that their mechanical, electrical and chem properties are sufficiently anisotropic to provide improved characteristics over conventional materials. Further, the shaped article and sinter thereof are improved in fracture toughness.

Detailed Description Paragraph Table (2):

Composition	Amount
Hydroxyapatite	40%
Water	50%
Pullulan	10%

CLAIMS:

1. A process for producing an oriented shaped article of a calcium phosphate compound, which process comprises: mixing an organic binder and water or an organic solvent with a powder of a calcium phosphate compound comprising rod-shaped crystal grains extending in the direction of one crystallographic axis thereof, kneading the mixed components, and extruding the resulting composition in a specified directi to shape said composition.

4. The process of claim 1, wherein the calcium phosphate compound is hydroxyapatite.

7. The process of claim 1, wherein the composition which is extruded comprises hydroxyapatite, water, butyl alcohol, methyl cellulose, a wa emulsion and a stearic acid emulsion.

8. The process of claim 1, wherein the composition which is extruded comprises hydroxyapatite, butyl methacrylate, an ethylene-vinyl acetat copolymer, a wax emulsion, dibutyl phthalate and stearic acid.

9. A process for producing an oriented sinter of a calcium phosphate compound, which process comprises: mixing an organic binder and wa or an organic solvent with powder of the calcium phosphate compound comprising rod-shaped crystal grains extending in the direction of on crystallographic axis thereof, kneading the mixed components, extruding the resulting composition in a specified direction to shape said composition, thermally decomposing the organic binder, and firing the shaped article at a temperature of from 900.degree. to 1,400.degree. C

12. The process of claim 9, wherein the calcium phosphate compound is hydroxyapatite.

15. The process of claim 9, wherein the composition which is extruded comprises hydroxyapatite, water, butyl alcohol, methyl cellulose, a w emulsion and a stearic acid emulsion.

16. The process of claim 9, wherein the composition which is extruded comprises hydroxyapatite, butyl methacrylate, an ethylene-vinyl acet copolymer, a wax emulsion, dibutyl phthalate and stearic acid.

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L8: Entry 37 of 48 File: USPT

US-PAT-NO: 5134009
DOCUMENT-IDENTIFIER: US 5134009 A

TITLE: Shaped article of oriented calcium phosphate type compounds, sinter thereof and processes for producing same

DATE-ISSUED: July 28, 1992

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ichitsuka; Takeshi	Tokyo			JP
Ogawa; Tetsuro	Tokyo			JP
Sumita; Masaya	Tokyo			JP
Yokoo; Akihiko	Tokyo			JP

US-CL-CURRENT: 428/113; 428/105, 428/221, 428/372, 428/373, 428/688, 428/704

CLAIMS:

What is claimed is:

1. An oriented shaped article of a calcium phosphate compound comprising primary particles of said calcium phosphate compound having at least two crystallographic axes, wherein at least two o said axes are oriented in one direction in at least a surface portion of said article.

2. An oriented shaped article of a calcium phosphate compound as claimed in claim 1, wherein said at least two of said axes are oriented in one direction i the entire article.

3. An oriented sinter of a calcium phosphate compound comprising primary particles of aid calcium phosphate compound having at least two crystallographic axes, wherein at least two of said axe are oriented in one direction in at least a surface portion of said sinter.

4. An oriented sinter of a calcium phosphate compound as claimed in claim 3, wherein at least two of said axes are oriented in one direction in the entire sinter.

WEST

Generate Collection Print

L8: Entry 37 of 48 File: USPT

DOCUMENT-IDENTIFIER: US 5134009 A
TITLE: Shaped article of oriented calcium phosphate type compounds, sinter thereof and processes for producing same

Abstract Text (1):
An oriented shaped article of a calcium phosphate type compound is disclosed, in which at least two crystallographic axes of the primary particles of which the shaped article is composed each is oriented in one direction, respectively, in at least the surface of said article. A sinte the oriented shaped article and a processes for producing the article and the sinter are also disclosed.

Brief Summary Text (2):
The present invention relates to shaped articles of calcium phosphate type compounds useful as biomaterials (e.g., artificial teeth and bones) as materials for humidity sensors, filters or IC substrates. The present invention also relates to sinters of these shaped articles and processes f producing the shaped articles and the sinters.

Brief Summary Text (4):
Due to their high biocompatibility, calcium phosphate type ceramics have conventionally been used as biomaterials such as artificial tooth ro and bones. Because the crystal particles (primary particles) of these ceramics are unoriented and these ceramics are unoriented polycrystallin bodies, the mechanical properties of these ceramics are isotropic. When these ceramics are placed under stress, the propagation of a fracture will travel over the shortest distance irrespective of the direction in which the stress is applied and the surface energy for a fracture becomes small that it will eventually cause a reduction in the fracture toughness of a shaped article of these ceramics and hence sinters thereof. Attem have been made to increase the strength of these ceramics by sintering them for high density after performing a suitable treatment such as HI (hot isotactic press), but no success has been achieved in improving their fracture toughness (as described, e.g., in Preprints of Annual Meeti of the Ceramics Society of Japan 1984, 3G10, pp. 939, published on May 14, 1984).

Brief Summary Text (5):
Hydroxyapatite which is in the class of calcium phosphate type compounds has ionic conductivity and research has been undertaken to study use as an electronic material in devices such as humidity sensors. However, conventional hydroxyapatite ceramics are also isotropic with res to electrical properties, and conduction ions in the ceramics are diffused at grain boundaries, making it impossible to provide satisfactory conductivity to the ceramics (As described, e.g., in Preprints of 2nd Apatite Meeting, pp. 22, published on Dec. 1, 1986).

Brief Summary Text (6):
In order to exploit the above various properties of calcium phosphate type ceramics in an advantageous way, it is necessary that shaped artic or sinters thereof have anisotropy. The ideal method for meeting this need would be to use single crystals of these ceramics. However, it is generally difficult to prepare large single crystals of calcium phosphate, and, in fact, no report has been published that describes success in preparing large single crystals of calcium phosphate.

Brief Summary Text (7):
In order to attain anisotropy for various properties of shaped articles and sinters, it is necessary that at least two crystallographic axes or at le two crystal faces each must be oriented in one direction, respectively. For example, in tubular bones of animals, the c axis of apatite crystals the bone is oriented in the direction parallel to the longitudinal direction of the bone, and the a axis thereof is oriented in the direction perpendicular to the longitudinal direction of the bone, by which the anisotropy of the mechanical properties is attained.

Brief Summary Text (8):
Hydroxyapatite sinters in which one crystal face of the crystalline particles is oriented by hot-pressing has been reported in Preprints of Annu Meeting of the Ceramic Society of Japan 1984, A-72, pp. 511, published on May 14, 1984. In this method, because tabular (plate-like) cryst are used, the (h00) plane is oriented in the pressing direction, but there is no research whether other planes (such as the (001) plane) are orien in one direction. Therefore, it is unknown whether sinters having anisotropy for mechanical properties are obtained by this method.

Brief Summary Text (10):
The present inventors therefore conducted intensive studies in order to develop calcium phosphate type ceramics in which the crystal grains

(i.e., the primary particles) are oriented in one direction and thus succeeded in reaching the present invention.

Brief Summary Text (11):
One object of the present invention is to provide a shaped article of an oriented calcium phosphate type compound.

Brief Summary Text (12):
Another object of the present invention is to provide a sinter of a shaped article of an oriented calcium phosphate type compound.

Brief Summary Text (15):
The present invention provides a shaped article of a calcium phosphate type compound in which at least two crystallographic axes of the primary particles which make up the shaped article each is oriented in one direction, respectively, in at least the surface of the article. Such orientation can be throughout the entire article.

Brief Summary Text (16):
Such an oriented shaped article of a phosphate type compound can be produced by a process which comprises mixing an organic binder and water or an organic solvent with a powdered calcium phosphate type compound comprising rod-shaped crystal grains extending in the direct of one crystallographic axis thereof, kneading the mixed components, and extruding the resulting clay-like composition in a specified directi to shape the composition.

Brief Summary Text (17):
The present invention also provides an oriented sinter of a calcium phosphate type compound in which at least two crystallographic axes of t primary particles which make up the sinter each is oriented in one direction, respectively, in at least the surface of the sinter. The entire sinte can be oriented.

Brief Summary Text (18):
Such an oriented sinter of a calcium phosphate type compound can be produced by a process comprising mixing an organic binder and wate an organic solvent with a powdered calcium phosphate type compound comprising rod-shaped crystal grains extending in the direction of on crystallographic axis, kneading the mixed components, extruding the resulting clay-like composition in a specified direction to shape the composition, thermally decomposing the organic binder, and firing the shaped article at a temperature of from 900.degree. to 1,400.degree. C

Detailed Description Text (2):
Examples of the calcium phosphate type compound of the present invention include hydroxyapatite, fluoroapatite, chloroapatite and tricalciu phosphate.

Detailed Description Text (3):
A commonly employed method for orienting grains in the direction of a certain crystallographic axis is by utilizing the electric or magnetic polarity of the grains. This method, however, is not highly effective in orienting the crystals of calcium phosphate type compounds because t polarity is rather low.

Detailed Description Text (4):
If calcium phosphate type compounds are synthesized by a wet method under properly selected conditions, it is possible to prepare rod-like crystal grains that are elongate in the direction of the c-axis as described in J. Am. Chem. Soc., Oct. 25, 1967, pp. 5535-5541. For instance, s grains can be synthesized by mixing a calcium compound with a phosphoric acid compound, the pH of the reaction solution being adjusted t either neutral or alkaline with the temperature held in the range of from 10.degree. to 100.degree. C. The ratio of the long axis to the short ax of the rod-like grains is preferably 1.1 or more, more preferably 1.5 or more, and particularly preferably 2.0 or more.

Detailed Description Text (7):
The secondary particles of a calcium phosphate type compound can be pulverized into primary particles when they are mixed with an organi binder and water or an organic solvent. If the slurry is not dried but is subjected to filtration, no secondary particles will form and the synthesized crystal grains may be directly used without being pulverized.

Detailed Description Text (8):
Therefore, in accordance with the present invention, the rod-shaped crystal grains of a calcium phosphate type compound are used as a starti powder, which is mixed with suitable amounts of a heat-decomposable organic binder and water or an organic solvent, as well as optionally with other additives such as a dispersant and a plasticizer. The ingredients are kneaded and the resulting clay-like composition is extruded to shape the same.

Detailed Description Text (16):
A slurry of hydroxyapatite synthesized by a conventional wet method (as described in J. Am. Chem. Soc., Oct. 25, 1967, pp. 5535-5541) wa spray-dried to make a powder having an average particle size of about 7 .mu.m. Observation under a scanning electron microscope showed t the powder was composed of spherical secondary particles which were dense agglomerations of elongate primary grains having a width of fr

200 to 500 .ANG. and length of about 1,000 .ANG.. These particles were calcined at 700.degree. C. for 4 hours and pulverized with a supersonic mill (product of Nippon Pneumatic Co., Ltd.) to obtain a fine powder having an average particle size of about 1 .mu.m. This fine powder (feed powder) was used as a starting material for the next shaping step.

Detailed Description Text (19):
The "degree of orientation" of hydroxyapatite as defined below is shown in Table 1 for each sample. As one can see from Table 1, the sinter the shaped articles prepared in Example 1 had the c-axis of the primary particles oriented in the direction of extrusion. However, the pulveriz products of these sinters showed no appreciable orientation and the relative intensities of individual diffraction lines were in accord with the data of ASTM 24-33.

Detailed Description Text (20):
The "degree of orientation" of hydroxyapatite as used herein is defined by ##EQU1## wherein I.sub.(300) is the diffraction intensity from th (300) face of a sample, and I.sub.(002) is the diffraction intensity from the (002) face of the sample. The ASTM value for I.sub.(300) /I.sub.(002) is 1.5.

Detailed Description Text (27):
A slurry containing 4% hydroxyapatite particles (based on total slurry weight) with a width of from 200 to 500 .ANG. and a length of about 1,000 .ANG. was obtained by a conventional wet method of synthesis (as described in J. Am. Chem. Soc., Oct. 25, 1967, pp. 5535-5541). T slurry was concentrated by filtration, and the following composition was obtained.

Detailed Description Text (28):
The composition containing the thus synthesized rod-shaped crystals of hydroxyapatite, a binder and water was spun by extrusion through an nozzle (diameter: 0.3 mm) at an air pressure of 900 mmH.sub.2 O according to JP-A-61-106166, and dried with hot air at 300.degree. C. to form a gauze-like shaped article. The dried article was sintered at 1,100.degree. C. for 4 hours and subjected to X-ray diffractiometry to chec for the occurrence of orientation. When an unpulverized sample of the gauze-like article was loaded in a glass sample holder, grain orientatio was observed in the same manner as in Examples 1 and 2.

Detailed Description Text (35):
An hydroxyapatite cylindrical molded article, which was molded, dried and degreased in the same manner as in Example 1, was fired at 1,100.degree. C. to obtain a siner. The sinter was cut in the direction parallel to the molding direction or in the direction perpendicular to the molding direction. The cut surfaces were polished and measured for X-ray diffraction scans. The X-ray diffraction scan for the cut surface parallel to the molding direction is shown in FIG. 7. The X-ray diffraction scan for the cut surface perpendicular to the molding direction is shown in FIG. 8. Separately, the sinter was pulverized in a mortar and measured for an X-ray diffraction scan which is shown in FIG. 9.

Detailed Description Text (39):
An hydroxyapatite plate-like molded article, which was molded, dried and degreased in the same manner as in Example 4, was fired at 1,100.degree. C. to obtain a sinter. From the measurement of X-ray diffraction scans, it was found that the sinter had the same orientation properties as in the sinter obtained in Example 4.

Detailed Description Text (52):
In accordance with the present invention, a certain crystallographic axis of the primary particles in at least the surface or the entire portion of shaped article to be produced can be oriented in one direction by a simple method. The shaped article of a calcium phosphate calcium compound or the sinter thereof which is produced by the present invention has grain orientation so that their mechanical, electrical and chem properties are sufficiently anisotropic to provide improved characteristics over conventional materials. Further, the shaped article and sinter thereof are improved in fracture toughness.

Detailed Description Paragraph Table (2):
____________________________________ Composition Amount ____________________________________ Hydroxyapatite 40% Water 50% Pullulan 10% ____________________________________

CLAIMS:

1. An oriented shaped article of a calcium phosphate compound comprising primary particles of said calcium phosphate compound having a least two crystallographic axes, wherein at least two of said axes are oriented in one direction in at least a surface portion of said article.

2. An oriented shaped article of a calcium phosphate compound as claimed in claim 1, wherein said at least two of said axes are oriented in o direction i the entire article.

3. An oriented sinter of a calcium phosphate compound comprising primary particles of aid calcium phosphate compound having at least two crystallographic axes, wherein at least two of said axes are oriented in one direction in at least a surface portion of said sinter.

4. An oriented sinter of a calcium phosphate compound as claimed in claim 3, wherein at least two of said axes are oriented in one direction the entire sinter.

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L8: Entry 47 of 48 File: DWPI Dec 17, 2001

DERWENT-ACC-NO: 2002-056540
DERWENT-WEEK: 200225

TITLE: Dental ceramic used in dentistry as filling material and tooth replacement is anisotropic and contains a large amount of hydroxylapa

INVENTOR: WIEDEMANN, W

PRIORITY-DATA: 2000DE-1027946 (June 8, 2000)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
AU 200174087 A	December 17, 2001		000	A61K006/033
DE 10027946 A1	December 13, 2001		008	A61K006/02
WO 200193808 A1	December 13, 2001	G	000	A61K006/033

INT-CL (IPC): A61 K 6/02; A61 K 6/033

ABSTRACTED-PUB-NO: DE 10027946A
BASIC-ABSTRACT:

NOVELTY - Dental ceramic is anisotropic and contains more than 90 wt.% hydroxylapatite ($Ca5(PO4)3OH$).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(a) a process for the production of the dental ceramic comprising precipitating at least one calcium phosphate compound from an aqueous or organo-aqueous solution to form a precipitate; optionally washing, drying and crushing the precipitate; pressing to form a green body; and sintering. The Ca/P atomic ratio is 1.66-1.68; and

(b) a crystalline hydroxylapatite having rod-like crystals with a length of 70-1000 nm and a thickness of 7-500 nm.

Preferred Features: The refractive index in the region of the visible light is anisotropic and the green body and/or the sintered body have a double refraction. The difference in the refractive index Delta n at least 1 x 10-4, especially at least 2 x 10-3. The anisotropy is vertical to a given axis. The amount of tricalcium phosphate and/or other sparingly soluble phosphate is not more than 4%.

USE - Used in dentistry as filling material and tooth replacement.

ADVANTAGE - The ceramic has similar properties to natural tooth enamel.

ABSTRACTED-PUB-NO: DE 10027946A
EQUIVALENT-ABSTRACTS:

CHOSEN-DRAWING: Dwg.0/1

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L8: Entry 47 of 48 File: DWPI Dec 17, 2001

DERWENT-ACC-NO: 2002-056540
DERWENT-WEEK: 200225

TITLE: Dental ceramic used in dentistry as filling material and tooth replacement is anisotropic and contains a large amount of hydroxylapa

INVENTOR: WIEDEMANN, W

PATENT-ASSIGNEE: HERAEUS KULZER GMBH & CO KG (HERA), WIEDEMANN W (WIEDI)

PRIORITY-DATA: 2000DE-1027946 (June 8, 2000)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
AU 200174087 A	December 17, 2001		000	A61K006/033
DE 10027946 A1	December 13, 2001		008	A61K006/02
WO 200193808 A1	December 13, 2001	G	000	A61K006/033

DESIGNATED-STATES: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW

APPLICATION-DATA:

PUB-NO	APPL-DATE	APPL-NO	DESCRIPTOR
AU 200174087A	June 6, 2001	2001AU-0074087	
AU 200174087A		WO 200193808	Based on
DE 10027946A1	June 8, 2000	2000DE-1027946	
WO 200193808A1	June 6, 2001	2001WO-EP06401	

INT-CL (IPC): A61 K 6/02; A61 K 6/033

ABSTRACTED-PUB-NO: DE 10027946A
BASIC-ABSTRACT:

NOVELTY - Dental ceramic is anisotropic and contains more than 90 wt.% hydroxylapatite ($Ca5(PO4)3OH$).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(a) a process for the production of the dental ceramic comprising precipitating at least one calcium phosphate compound from an aqueous or organo-aqueous solution to form a precipitate; optionally washing, drying and crushing the precipitate; pressing to form a green body; and sintering. The Ca/P atomic ratio is 1.66-1.68; and

(b) a crystalline hydroxylapatite having rod-like crystals with a length of 70-1000 nm and a thickness of 7-500 nm.

Preferred Features: The refractive index in the region of the visible light is anisotropic and the green body and/or the sintered body have a double refraction. The difference in the refractive index Delta n at least 1 x 10-4, especially at least 2 x 10-3. The anisotropy is vertical to a given axis. The amount of tricalcium phosphate and/or other sparingly soluble phosphate is not more than 4%.

USE - Used in dentistry as filling material and tooth replacement.

ADVANTAGE - The ceramic has similar properties to natural tooth enamel.

ABSTRACTED-PUB-NO: DE 10027946A
EQUIVALENT-ABSTRACTS:

CHOSEN-DRAWING: Dwg.0/1

DERWENT-CLASS: D21 L02
CPI-CODES: D08-A03; L02-A04; L02-G03A1; L02-G08;

WEST

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L8: Entry 47 of 48 File: DWPI Dec 17, 2001

DERWENT-ACC-NO: 2002-056540
DERWENT-WEEK: 200225

TITLE: Dental ceramic used in dentistry as filling material and tooth replacement is anisotropic and contains a large amount of hydroxylapa

Basic Abstract Text (1):
NOVELTY - Dental ceramic is anisotropic and contains more than 90 wt.% hydroxylapatite ($Ca5(PO4)3OH$).

Basic Abstract Text (3):
(a) a process for the production of the dental ceramic comprising precipitating at least one calcium phosphate compound from an aqueous or organo-aqueous solution to form a precipitate; optionally washing, drying and crushing the precipitate; pressing to form a green body; and sintering. The Ca/P atomic ratio is 1.66-1.68; and

Basic Abstract Text (4):
(b) a crystalline hydroxylapatite having rod-like crystals with a length of 70-1000 nm and a thickness of 7-500 nm.

Basic Abstract Text (5):
Preferred Features: The refractive index in the region of the visible light is anisotropic and the green body and/or the sintered body have a double refraction. The difference in the refractive index Delta n at least 1 x 10-4, especially at least 2 x 10-3. The anisotropy is vertical to a given axis. The amount of tricalcium phosphate and/or other sparingly soluble phosphate is not more than 4%.

Standard Title Terms (1):
DENTAL CERAMIC DENTIST FILL MATERIAL TOOTH REPLACE ANISOTROPE CONTAIN AMOUNT

WEST

End of Result Set

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L8: Entry 48 of 48 File: DWPI Jan 24, 1996

DERWENT-ACC-NO: 1990-085096
DERWENT-WEEK: 199608

TITLE: Shaped articles of oriented calcium phosphate type cpd. - obtd. by extrusion of compsn. contg. oriented grains, used for dental and orthopaedic prosthesis, IC substrates etc.

INVENTOR: ICHITSUKA, T; OGAWA, T ; SUMITA, M ; YOKOO, A

PRIORITY-DATA: 1988JP-0230570 (September 15, 1988)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
JP 96005712 B2	January 24, 1996		007	C04B035/447
EP 359278 A	March 21, 1990	E	017	
JP 02080361 A	March 20, 1990		000	
US 5134009 A	July 28, 1992		014	C07C061/06
US 5240659 A	August 31, 1993		015	C04B035/64
CA 1332867 C	November 8, 1994		000	C04B035/00

INT-CL (IPC): A61L 27/00; B29C 67/00; C01B 25/32; C04B 35/00; C04B 35/447; C04B 35/64; C07C 61/06

ABSTRACTED-PUB-NO: EP 359278A
BASIC-ABSTRACT:

In a shape article of a calcium phosphate-type cpd. at least two crystallographic axes of the primary particles constituting the article are each aligned in the surface of the latter, and pref. throughout it.

The article is formed by mixing an organic binder with water or organic solvent and a powder of the cpd. comprising rod-shaped grains havi their aces parallel to one crystallographic axes. The mixture is kneaded and extruded. The product may be heated to eliminate the binder and then sintered at 900-1400 deg.C.

USE/ADVANTAGE - Used in dental or orthopaedic prostheses; humidity sensors; filters; I.C. substrates. Product is suitable for many applications which require anisotropic properties.

ABSTRACTED-PUB-NO:

US 5134009A
EQUIVALENT-ABSTRACTS:

Article is composed of prim. particles of Ca phosphate having at least two crystallographic axes, oriented in one direction in at least a surfac portion of the article, and opt. in the entire article. Oriented sinter of the above Ca phosphate particles is also described. USE/ADVANTAGE Used as biomaterials (e.g. artificial teeth and bones) or as materials for humidity sensors, filters or IC substrates. Anisotropy of the mechanic properties is obtd.

ABSTRACTED-PUB-NO: EP 359278A
EQUIVALENT-ABSTRACTS: US 5134009A Article is composed of prim. particles of Ca phosphate having at least two crystallographic a oriented in one direction in at least a surface portion of the article, and opt. in the entire article. Oriented sinter of the above Ca phosphate particles is also described. USE/ADVANTAGE - Used as biomaterials (e.g. artificial teeth and bones) or as materials for humidity sensors, filters or IC substrates. Anisotropy of the mechanical properties is obtd.

CHOSEN-DRAWING: Dwg.1/9 Dwg.0/0

WEST

End of Result Set

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L8: Entry 48 of 48 File: DWPI Jan 24, 1996

DERWENT-ACC-NO: 1990-085096
DERWENT-WEEK: 199608

TITLE: Shaped articles of oriented calcium phosphate type cpd. - obtd. by extrusion of compsn. contg. oriented grains, used for dental and orthopaedic prosthesis, IC substrates etc.

Basic Abstract Text (1):
In a shape article of a calcium phosphate-type cpd. at least two crystallographic axes of the primary particles constituting the article are each aligned in the surface of the latter, and pref. throughout it.

Basic Abstract Text (3):
USE/ADVANTAGE - Used in dental or orthopaedic prostheses; humidity sensors; filters; I.C. substrates. Product is suitable for many applications which require anisotropic properties.

Equivalent Abstract Text (1):
Article is composed of prim. particles of Ca phosphate having at least two crystallographic axes, oriented in one direction in at least a surfac portion of the article, and opt. in the entire article. Oriented sinter of the above Ca phosphate particles is also described. USE/ADVANTAGE Used as biomaterials (e.g. artificial teeth and bones) or as materials for humidity sensors, filters or IC substrates. Anisotropy of the mechanic properties is obtd.

Standard Title Terms (1):
SHAPE ARTICLE ORIENT CALCIUM PHOSPHATE TYPE COMPOUND OBTAIN EXTRUDE COMPOSITION CONTAIN ORIENT GRAIN DENTAL ORTHOPAEDIC PROSTHESIS IC SUBSTRATE

WEST

End of Result Set

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L8: Entry 48 of 48 File: DWPI Jan 24, 1996

DERWENT-ACC-NO: 1990-085096
DERWENT-WEEK: 199608

TITLE: Shaped articles of oriented calcium phosphate type cpd. - obtd. by extrusion of compsn. contg. oriented grains, used for dental and orthopaedic prosthesis, IC substrates etc.

INVENTOR: ICHITSUKA, T; OGAWA, T ; SUMITA, M ; YOKOO, A

PATENT-ASSIGNEE: ASAHI KOGAKU KOGYO KK (ASAO), ASAHI KOGAKU KKGYO KK (ASAO)

PRIORITY-DATA: 1988JP-0230570 (September 15, 1988)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
JP 96005712 B2	January 24, 1996		007	C04B035/447
EP 359278 A	March 21, 1990	E	017	
JP 02080361 A	March 20, 1990		000	
US 5134009 A	July 28, 1992		014	C07C061/06
US 5240659 A	August 31, 1993		015	C04B035/64
CA 1332867 C	November 8, 1994		000	C04B035/00

DESIGNATED-STATES: DE FR GB SE

CITED-DOCUMENTS:2.Jnl.Ref; A3...9102 ; EP 174827 ; FR 2249856 ; No-SR.Pub

APPLICATION-DATA:

PUB-NO	APPL-DATE	APPL-NO	DESCRIPTOR
JP96005712B2	September 15, 1988	1988JP-0230570	
JP96005712B2		JP 2080361	Based on
EP 359278A	September 15, 1989	1989EP-0117111	
JP02080361A	September 15, 1988	1988JP-0230570	
US 5134009A	September 14, 1989	1989US-0407009	
US 5240659A	September 14, 1989	1989US-0407009	Cont of
US 5240659A	March 24, 1992	1992US-0857638	
US 5240659A		US 5134009	Cont of
CA 1332867C	September 14, 1989	1989CA-0611444	

INT-CL (IPC): A61L 27/00; B29C 67/00; C01B 25/32; C04B 35/00; C04B 35/447; C04B 35/64; C07C 61/06

ABSTRACTED-PUB-NO: EP 359278A
BASIC-ABSTRACT:

In a shape article of a calcium phosphate-type cpd. at least two crystallographic axes of the primary particles constituting the article are each aligned in the surface of the latter, and pref. throughout it.

The article is formed by mixing an organic binder with water or organic solvent and a powder of the cpd. comprising rod-shaped grains havi their aces parallel to one crystallographic axes. The mixture is kneaded and extruded. The product may be heated to eliminate the binder and then sintered at 900-1400 deg.C.

USE/ADVANTAGE - Used in dental or orthopaedic prostheses; humidity sensors; filters; I.C. substrates. Product is suitable for many applications which require anisotropic properties.

ABSTRACTED-PUB-NO: US 5134009A
EQUIVALENT-ABSTRACTS:

Article is composed of prim. particles of Ca phosphate having at least two crystallographic axes, oriented in one direction in at least a surfac portion of the article, and opt. in the entire article. Oriented sinter of the above Ca phosphate particles is also described. USE/ADVANTAGE Used as biomaterials (e.g. artificial teeth and bones) or as materials for humidity sensors, filters or IC substrates. Anisotropy of the mechanic properties is obtd.

CHOSEN-DRAWING: Dwg.1/9 Dwg.0/0

DERWENT-CLASS: D21 D22 L02 L03 P34 U11
CPI-CODES: D08-A03; D09-C01; L02-G03A;
EPI-CODES: U11-A05B; U11-B03;

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Search Results -

Term	Documents
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WETTING.DWPI,TDBD,EPAB,JPAB,USPT.	123959
PROTECTIVE.DWPI,TDBD,EPAB,JPAB,USPT.	484209
SURFACTANT?	0
SURFACTANTA.DWPI,TDBD,EPAB,JPAB,USPT.	9
SURFACTANTE.DWPI,TDBD,EPAB,JPAB,USPT.	3
SURFACTANTG.DWPI,TDBD,EPAB,JPAB,USPT.	2
SURFACTANTI.DWPI,TDBD,EPAB,JPAB,USPT.	1
SURFACTANTM.DWPI,TDBD,EPAB,JPAB,USPT.	1
SURFACTANTN.DWPI,TDBD,EPAB,JPAB,USPT.	1
(L13 AND (SURFACTANT? OR SURFACE ACTIVE AGENT? OR WETTING AGENT? OR PROTECTIVE COLLOID?)).USPT,JPAB,EPAB,DWPI,TDBD.	22

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DATE: Wednesday, July 31, 2002 Printable Copy Create Case

Set Name side by side	**Query**	**Hit Count**	**Set Name** result s
	DB=USPT,JPAB,EPAB,DWPI,TDBD; PLUR=NO; OP=ADJ		
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L13	111 and agglomerat?	37	L13
L12	111 and particle?.clm.	126	L12
L11	110 and (nano?.clm. or nm.clm. or nanometers.clm. or nanometer?.clm.)	416	L11
L10	11 and (whiskers or rodlike or barlike or needle crystals or particle length? or nanometers or nanocrystals or nanoparticles or rod-shaped or bar-shaped or 20nm or 70 nm or 5 nm or 10 nm or 40 nm or 50 nm or 35 nm or 30 nm or 130 nm or 50 nanometers or 150 nanometers)	3756	L10
L9	18 and diameter? and length?	12	L9
L8	13 and (toothpaste or dentifrice or stomatol? or teeth or dental)	48	L8
L7	15 and 12	0	L7
L6	15 and nano?.clm.	0	L6
L5	11 and nano?	35	L5
L4	13 and crystals and particle size	32	L4
L3	11 and (anisometric or anisotropic)	307	L3
L2	11 and agglomeration	879	L2
L1	(calcium phosphate or apatite or hydroxylapatite or hydroxyapatite or calcium fluoride or fluorapatite o0r amorphous calcium phosphate or fluorophosphate calcium or calcium fluorophosphate or fluorine-doped hydroxylapatite or f-doped hydroxylapatite)	47239	L1

END OF SEARCH HISTORY

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L14: Entry 13 of 22 File: USPT

US-PAT-NO: 6013591
DOCUMENT-IDENTIFIER: US 6013591 A

TITLE: Nanocrystalline apatites and composites, prostheses incorporating them, and method for their production

DATE-ISSUED: January 11, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ying; Jackie Y.	Winchester	MA		
Ahn; Edward S.	Cambridge	MA		
Nakahira; Atsushi	Kyoto			JP

US-CL-CURRENT: 501/1; 106/35, 423/308, 423/311, 424/422, 424/423, 427/2.27, 428/689, 428/704, 623/23.71, 623/23.76

CLAIMS:

What is claimed is:

1. A composition, comprising particulate apatite having an averag apatite crystal size of less than 100 nm, wherein the crystal is spherical.

2. The composition of claim 1 comprising particulate apatite having an average apatite crystal size of less than 50 nm.

3. The composition of claim 1 comprising particulate apatite having an average apatite crystal size of less than 30 nm.

4. The composition of claim 1 comprising particulate apatite having an average apatite crystal size of less than 20 nm.

5. A composition as in claim 1 wherein the particulate apatite is densified.

6. The composition of claim 1 comprising apatite having an averag particle size of less than 1 .mu.m.

7. The composition of claim 1 comprising apatite having an averag particle size of less than 0.5 .mu.m.

8. The composition of claim 1 comprising apatite having an averag

particle size of less than 0.25 .mu.m.

9. A composition comprising particulate apatite having a surface area of at least 40 m.sup.2 /g and a spherical crystal.

10. The composition of claim 7 comprising particulate apatite having a surface area of at least 100 m.sup.2 /g.

11. The composition of claim 9 comprising particulate apatite having a surface area of at least 150 m.sup.2 /g.

12. The composition of claim 9 that undergoes apatite phase decomposition of less than 10% when exposed to conditions of at least 1000.degree. C. for at least 2 hours.

13. The composition of claim 12 that undergoes apatite phase decomposition of less than 5% when exposed to conditions of at least 1000.degree. C. for at least 2 hours.

14. The composition of claim 12 that undergoes apatite phase decomposition of less than 3% when exposed to conditions of at least 1000.degree. C. for at least 2 hours.

15. The composition of claim 12 that undergoes apatite phase decomposition of less than 10% when exposed to conditions of at least 1100.degree. C. for at least 2 hours.

16. The composition of claim 12 that undergoes apatite phase decomposition of less than 5% when exposed to conditions of at least 1100.degree. C. for at least 2 hours.

17. The composition of claim 12 that undergoes apatite phase decomposition of less than 3% when exposed to conditions of at least 1100.degree. C. for at least 2 hours.

18. The composition of claim 12 that undergoes apatite phase decomposition of less than 10% when exposed to conditions of at least 1200.degree. C. for at least 2 hours.

19. The composition of claim 12 that undergoes apatite phase decomposition of less than 5% when exposed to conditions of at least 1200.degree. C. for at least 2 hours.

20. The composition of claim 12 that undergoes apatite phase decomposition of less than 3% when exposed to conditions of at least 1200.degree. C. for at least 2 hours.

21. The composition of claim 12 that undergoes apatite phase decomposition of less than 10% when exposed to conditions of at least 1300.degree. C. for at least 2 hours.

22. The composition of claim 12 that undergoes apatite phase decomposition of less than 5% when exposed to conditions of at least 1300.degree. C. for at least 2 hours.

23. The composition of claim 12 that undergoes apatite phase decomposition of less than 3% when exposed to conditions of at least 1300.degree. C. for at least 2 hours.

24. An article having a dimension of at least 0.5 cm made up of the composition of claim 1.

25. The article of claim 24 wherein the particulate apatite is consolidated.

26. The article of claim 24, formed into the shape of a prosthesis.

27. The article of claim 24 that is a prosthesis.

28. The article of claim 24 comprising an exterior coating on a prosthesis.

29. The article of claim 28 comprising an exterior coating, on a prosthesis, of at least 0.5 micron in thickness.

30. The article of claim 24 having a theoretical density of at least 90%.

31. The article of claim 24 having a theoretical density of at least 95%.

32. The article of claim 24 having a theoretical density of at least 98%.

33. An article having a dimension of at least 0.5 cm made up of the composition of claim 9.

34. The article of claim 33 having a porosity of at least 20%.

35. The article of claim 33 having a porosity of at least 30%.

36. The article of claim 33 having a porosity of at least 50%.

37. The article of claim 33 having a porosity of at least 75%.

38. The densified article of claim 33 having compressive strength of at least about 150 MPa.

39. The densified article of claim 38, having a density of at least about 98%.

40. The densified article of claim 33 having compressive strength of at least about 500 MPa.

41. The densified article of claim 33 having compressive strength of at least about 700 MPa.

42. The densified article of claim 38, having a density of at least about 90%.

43. The densified article of claim 38, having a density of at least about 95%.

44. The article of claim 24 that is a part of a prosthesis.

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L14: Entry 13 of 22 File: USPT Jan 11, 2000

US-PAT-NO: 6013591
DOCUMENT-IDENTIFIER: US 6013591 A

TITLE: Nanocrystalline apatites and composites, prostheses incorporating them, and method for their production

DATE-ISSUED: January 11, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ying; Jackie Y.	Winchester	MA		
Ahn; Edward S.	Cambridge	MA		
Nakahira; Atsushi	Kyoto			JP

ASSIGNEE-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY	TYPE CODE
Massachusetts Institute of Technology	Cambridge	MA			02

APPL-NO: 09/ 007930 [PALM]
DATE FILED: January 16, 1998

PARENT-CASE:
RELATED APPLICATION This non-provisional application claims the benefit under Title 35, U.S.C. .sctn.119(e) of co-pending U.S. provisional application serial No. 60/035,535, filed Jan. 16, 1997, entitled "Nanocrystalline Apatites and Composites, Prostheses Incorporat Them, and Method for Their Production" by Jackie Y. Ying et al., incorporated herein by reference.

INT-CL: [06] C01 B 15/16, A61 F 2/28, C04 B 35/01

US-CL-ISSUED: 501/1; 106/35, 423/308, 423/311, 428/689, 428/704, 623/11, 623/12, 427/2.27, 424/423, 424/422
US-CL-CURRENT: 501/1; 106/35, 423/308, 423/311, 424/422, 424/423, 427/2.27, 428/689, 428/704, 623/23.71, 623/23.76

FIELD-OF-SEARCH: 501/1, 423/308, 423/311, 106/35, 428/689, 428/704, 623/11, 623/16, 427/2.27, 424/423, 424/422

PRIOR-ART-DISCLOSED:

U.S. PATENT DOCUMENTS

Search Selected | Search ALL

	PAT-NO	ISSUE-DATE	PATENTEE-NAME	US-CL
☐	4097935	July 1978	Jarcho	106/35
☐	4195366	April 1980	Jarcho et al.	106/35
☐	4207306	June 1980	Jarcho	423/633
☐	4330514	May 1982	Nagai et al.	423/311
☐	4497075	February 1985	Niwa et al.	501/1
☐	5030474	July 1991	Saita et al.	427/2.27
☐	5134009	July 1992	Ichitsuka et al.	428/113
☐	5405436	April 1995	Maurer et al.	102/35
☐	5427754	June 1995	Nagata et al.	423/308
☐	5470803	November 1995	Bonfield et al.	501/1
☐	5501706	March 1996	Arenberg	623/16
☐	5522893	June 1996	Chow et al.	623/4
☐	5542973	August 1996	Chow et al.	106/35
☐	5545254	August 1996	Chow et al.	106/35
☐	5667796	September 1997	Otten	424/422

OTHER PUBLICATIONS

R.W. Siegel, "Recent Progress in Nanophase Materials", Processing and Properties of Nanocrystalline Materials, C.Suryanarayana, J.Singh F.H.Froes, Eds., The Minerals, Metals & Materials Society, 1996, no month.
L.L. Hench, "Bioceramics: From Concept to Clinic", American Ceramic Society Bulletin, vol. 72, No. 4, pp. 93-98 (Apr. 1993).
L.L. Hench, "Bioceramics: From Concept to Clinic", J. Am. Ceram. Soc. 74 [7], pp. 1487-1510 (1991), no month.
L.L. Hench and J. Wilson, An Introduction to Bioceramics, Chapter 1 "Introduction", pp. -124, L.L. Hench and J. Wilson, Eds., 1993. no month.
J.D. deBruijn et al., "Biological Responses to Calcium Phosphate Ceramics", Bone-Bonding--Reed Healthcare Communications, Ducheyne, Kokubo & Van Blitterswijk, Eds., pp. 57-72, 1992, no month.
M. Akao, et al., "Dense Polycrystalline .beta.-Tricalcium Phosphate For Prosthetic Applications," J. of Materials Science, 17, pp. 343-346, 1982, no month.
M. Jarcho, et al., "Hydroxylapatite Synthesis and Characterization in Dense Polycrystalline Form", J. of Materials Science, 11, pp. 2027-203 (1976), no month.
M. Akao et al., "Mechanical Properties of Sintered Hydroxyapatite for Prosthetic Applications", J. of Materials Science, 16, pp. 809-812 (1981), no month.
K. Niihara, et al., "New Nanocomposite Structural Ceramics", Nanophase and Nanocomposite Materials, S. Komarneni, J.C. Parker, G.J. Thomas, Eds., Mat. Res. Soc. Symp Proc., vol. 286, pp. 405-412 (1993), no month.

ART-UNIT: 175

PRIMARY-EXAMINER: Koslow; C. Melissa

ABSTRACT:

Methods for synthesis of nanocrystalline apatites are presented, as well as a series of specific reaction parameters that can be adjusted to tail in specific ways, properties in the recovered product. Particulate apatite compositions having average crystal size of less than 150 nm are provided. Products also can have a surface area of at least 40 m.sup.2 /g and can be of high density.

Hydroxyapatite material is investigated in particular detail. Compositions of the invention can be used as prosthetic implants and coatings fo prosthetic implants.

44 Claims, 0 Drawing figures

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L14: Entry 13 of 22 File: USPT

DOCUMENT-IDENTIFIER: US 6013591 A
TITLE: Nanocrystalline apatites and composites, prostheses incorporating them, and method for their production

Abstract Text (1):
Methods for synthesis of nanocrystalline apatites are presented, as well as a series of specific reaction parameters that can be adjusted to tail in specific ways, properties in the recovered product. Particulate apatite compositions having average crystal size of less than 150 nm are provided. Products also can have a surface area of at least 40 m.sup.2 /g and can be of high density.

Abstract Text (2):
Hydroxyapatite material is investigated in particular detail. Compositions of the invention can be used as prosthetic implants and coatings fo prosthetic implants.

Brief Summary Text (2):
The present invention relates generally to bioceramics and more particularly to a class of apatite materials and composites incorporating thes materials that are useful as prostheses, or coatings for prosthesis, and methods for production of these materials.

Brief Summary Text (7):
Bioceramics have found widespread use in periodontic and orthopedic applications as well as oral, plastic, and ear, nose, and throat surgery. Common materials for bioceramics are alumina, zirconia, calcium phosphate based ceramics, and glass-ceramics. Bioceramics can be categorized according to their in vivo interaction, typically as bioinert, bioactive, and resorbable bioceramics. Various types of bioceramics undergo fixation within the body according to different processes. Some processes are generally more favorable than others, but in many cas bioceramic material that undergoes fixation within the body via one advantageous interaction may be associated with other disadvantages.

Brief Summary Text (9):
Resorbable bioceramics include tricalcium phosphate, calcium sulfate, and calcium phosphate salt based bioceramics. They are used to repla damaged tissue and to eventually be resorbed such that host tissue surrounding an implant made of the resorbable ceramic eventually replace the implant.

Brief Summary Text (10):
Bioactive bioceramics include hydroxyapatite bioceramics, glass, and glass-ceramics. A "bioactive" material is one that elicits a specific biological response at its surface which results in the formation of a bond with tissue. Thus, bioactive materials undergo chemical reactions i the body, but only at their surfaces. These chemical reactions lead to chemical and biological bonding to tissue at the interface between tissu and a bioactive implant, rather than mere ingrowth of tissue into pores of the implant which provide mechanical fixation. A characteristic of bioactive ceramic articles is the formation of a hydroxycarbonate apatite (HCA) layer on the surface of the article. The degree of bioactivity measured in terms of the rate of formation of HCA, bonding, strength, and thickness of the bonding layer as well as cellular activity.

Brief Summary Text (15):
Hydroxyapatite, Ca.sub.10 (PO.sub.4).sub.6 (OH).sub.2, is an attractive and widely utilized bioceramic material for orthopedic and dental implants because it closely resembles native tooth and bone crystal structure. Though hydroxyapatite is the most common bioceramic, applications for its use have been limited by its processability and architectural design conceptualization. Conventional processing lacks compositional purity and homogeneity. Because hydroxyapatite is difficult to sinter, dense hydroxyapatite structures for dental implants and wear orthopedic applications typically have been obtained by high-temperature and/or high-pressure sintering with glassy sintering aids whic frequently induce decomposition to undesirable phases with poor mechanical stability and poor chemical resistance to physiological conditio Thus, conventionally-formed hydroxyapatite necessitates expensive processing and compromises structural integrity due to the presence of secondary phases. Existing methods require high forming and machining costs to obtain products with complex shapes. Furthermore, typical conventional hydroxyapatite decomposes above 1250.degree. C. This results in a material with poor mechanical stability and poor chemical resistance.

Brief Summary Text (16):

Jarcho, et al., in "Hydroxyapatite Synthesis and Characterization in Dense Polycrystalline Form", J. Mater. Sci., 11, 2027-2035 (1976)), describe a process for forming dense polycrystalline hydroxyapatite that is "substantially stronger than other hydroxyapatite materials", and elicits "an excellent biological response when implanted in bone" (p. 2027). A precipitation method was used and material of average grain s of from about 150-700 nm recovered. However, Jarcho, et al. report low volume fraction of pores, and report considerable grain growth duri sintering even at firing temperatures of 1000.degree. C. Jarcho, et al. achieved 99% density in some cases, but using a technique that can be impractical for forming desired shapes. M. Akao, et al., in "Mechanical Properties of Sintered Hydroxyapatite for Prosthetic Applications", J Mater. Sci., 16, 809-812 (1981), report the compressive flexural torsional and dynamic torsional strengths of polycrystalline hydroxyapatite sintered at 1300.degree. C. for three hours and, compare the mechanical properties of the product with those of cortical bone, dentine, and enamel. The compressive strength of the sintered hydroxy apatite was approximately 3-6 times as strong as that of cortical bone.

Brief Summary Text (17):
There is much room for improvement in the use of hydroxyapatite as implants. As reported by Hench et al., "Bioceramics: from concept to clinic", American Ceramic Society Bulletin 72, 4, 93-98 (1993), "Because (hydroxyapatite) implants have low reliability under tensile load, such calcium phosphate bioceramics can only be used as powders, or as small, unloaded implants such as in the middle ear, dental implants w reinforcing metal posts, coatings on metal implants, low-loaded porous implants where bone growth acts as a reinforcing phase, and as the bioactive phase in a composite." (p. 97). Hench, J. Am. Ceram Soc. (1991; referenced above) reports that hydroxyapatite has been used as a coating on porous metal surfaces for fixation of orthopedic prostheses, in particular, that hydroxyapatite powder in the pores of porous, coated-metal implants would significantly affect the rate and vitality of bone ingrowth into the pores. It is reported that many investigators h explored this technique, with plasma spray coating of implants generally being preferred. Hench reports, however, that long term animal stud and clinical trials of load-bearing dental and orthopedic prostheses suggest that the hydroxyapatite coatings may degrade or come off (p. 150 Thus, the creation of new forms of hydroxyapatite having improved mechanical properties would have significant use, but the results of prio attempts have been disappointing.

Brief Summary Text (18):
Recently, attention has been focused on nanocrystalline or nanocomposite materials for mechanical, optical and catalytic applications. By designing materials from the cluster level, crystallite building blocks of less than 10 nm are possible, through which unique size-dependent properties such as quantum confinement effect and superparamagnetism can be obtained. Various nanocrystalline ceramics for structural applications have been especially rigorously investigated in the 1990's. R. Siegel discusses nanophase metals and ceramics in "Recent Progre in Nanophase Materials", in Processing and Properties of Nanocrystalline Materials, C. Suryanarayana, et al., Ed., The Minerals, Metals & Materials Society (1996), noting that while many methods exist for the synthesis of nanostructured materials, including chemical or physical vapor deposition, gas condensation, chemical precipitation, aerosol reactions, and biological templating, synthesis and processing methods f creating tailored nanostructures are sorely needed, especially techniques that allow careful control of surface and interface chemistry and tha can lead to adherent surface coatings or well-consolidated bulk materials. It is noted that in the case of normally soft metals, decreasing grain sizes of the metal below a critical length scale (less than about 50 nm) for the sources of dislocations in the metal increases the metal's streng It is noted that clusters of metals, intermetallic compounds, and ceramics have been consolidated to form ultrafine-grained polycrystals that have mechanical properties remarkably different and improved relative to their conventional coarse-grained counterpart. Nanophase copper palladium, assembled from clusters with diameters in the range of 5-7 nm, are noted for having hardness and yield strength values up to 500% greater than in conventionally-produced metal. It is also noted that ceramics and conventionally brittle intermetallics can be rendered ductile being synthesized from clusters with sizes below about 15 nm, the ductility resulting from the increased ease with which the ultrafine grains slide by one another in "grain-boundary sliding." However, synthesis of nanocrystalline or nanocomposite materials is difficult. Significant effort has been put into such synthesis and it is likely that in many or most attempts particle sizes on the nanometer scale are not recovered d to agglomeration. A delicate balance of synthetic parameters typically must be elucidated in connection with a particular set of materials.

Brief Summary Text (20):
While hydroxyapatite is used widely, and a hydroxyapatite formulation having mechanical and morphological properties advantageous for prostheses would be very useful, attempts to date have failed to produce reliable structural hydroxyapatite implants. Accordingly, it is an obj of the invention to provide relatively simple techniques for synthesizing nanocrystalline apatite materials having structural and morphologica properties useful for structural implants. In particular, it is an object to provide synthesis techniques that produce densified, nanocrystalline material under mild conditions including relatively low sintering temperature, reducing or eliminating decomposition and minimizing cost. I another object to obtain apatite materials having enhanced mechanical and chemical resistance by maintaining an ultrafine microstructure in sintering through suppression of grain growth.

Brief Summary Text (22):
The present invention provides a set of compositions, articles, and methods involving apatite materials of particularly small crystal size and/ particle size that can be readily formed into a variety of products.

Brief Summary Text (23):
By carefully controlling processing parameters affecting the molecular and structural development of hydroxyapatite such as precursor type, precursor concentration, addition rate of precursors, aging time, reaction and aging temperature, and pH during synthesis, as well as by controlling parameters affecting the agglomeration of ceramic particles such as washing and drying of the as-synthesized gel, a loosely agglomerated nanocrystalline hydroxyapatite powder is obtained. By minimizing particle size, packing and densification is enhanced resultin

in the fabrication of densified nanocrystalline hydroxyapatite by using a simple pressureless sintering process at relatively low sintering temperatures. By reducing crystallite size, ceramics become more ductile as the volume fraction of grain boundaries increases allowing grain boundary sliding. Nanostructured hydroxyapatite also allows superplastic net-shape forming for inexpensive production. Furthermore, by achieving smaller crystallite sizes, defect size is reduced. With minimized flaw sizes, nanocrystalline hydroxyapatite is densified with minim or no sintering additives at substantially lower temperatures and demonstrates improved strength compared to the conventional polycrystallin hydroxyapatite. Thus, nanocrystalline hydroxyapatite possesses greater reliability and better mechanical properties compared to conventiona hydroxyapatite with a coarser microstructure. Additionally, hydroxyapatite can be structurally reinforced by nanocomposite processing such incorporating nanocrystalline zirconia into hydroxyapatite. Additionally, carbonate icons be substituted for phosphate ions in hydroxyapatite yield carbonate apatite, both Type A and Type B.

Brief Summary Text (24):
Using wet chemical processing as the basis, synthetic approaches to obtain a variety of products: hydroxyapatite, carbonate apatite, and fluoroapatite in the form of nanocrystalline dense structures as well as high surface area powders and coatings are developed by controlling t morphology, size, and reactivity of the precipitated particles. These novel materials possess high chemical purity and phase homogeneity wit tailored mechanical strength and biocompatibility. A wet chemical approach is used because it is versatile, simple, and easy to control, in ter of both the preparative reactions and the characteristics of the reaction product. Furthermore, the synthesis conditions of the wet chemical approach can be tailored to physiological conditions for biomimetic processing. When synthesized at low temperatures and at ambient pressu in an aqueous solution resembling physiological fluid, a bioactive hydroxyapatite stable in the body is produced.

Brief Summary Text (25):
In order to manipulate the processing of nanocrystalline hydroxyapatite, important processing parameters were identified. Parameters affecti the molecular and structural development, and chemistry of hydroxyapatite such as reaction and aging temperature, aging time, addition rate Ca(NO.sub.3).sub.2 to the basic (NH.sub.4).sub.2 HPO.sub.4 solution, NH.sub.4 OH concentration during chemical precipitation, and precursor concentration were examined. Parameters affecting the agglomeration and densification of ceramic particles such as grinding meth calcination temperature, and sintering temperature were also investigated. By reducing crystallite size, ceramics are toughened as the volume fraction of grain boundaries increases allowing grain boundary sliding. Furthermore, by achieving smaller crystallite sizes, defect size are reduced. By minimizing particle size, packing and densification can be enhanced.

Brief Summary Text (26):
In one aspect, the invention provides a composition including particulate apatite having an average apatite crystal size of less than 250 nm. I another embodiment, the invention provides an apatite composition having a surface area of at least 40 m.sup.2 /g.

Brief Summary Text (27):
The invention provides, according to another aspect, a method that involves precipitating apatite from a solvent as an apatite precipitate, removing the solvent from the apatite precipitate, and recovering the precipitate, particulate apatite. In the method, the recovered particulate apatite has an average crystal size of less than 150 nm.

Brief Summary Text (28):
The invention also provides a method of calcining nanocrystalline apatite at a temperature of less than 1000.degree. C. and recovering a nanostructured apatite product having a BET surface area of at least 40 m.sup.2 /g and a crystal size of less than 500 nm.

Brief Summary Text (29):
In another aspect the invention provides a particulate apatite composition having an average crystal size small enough that the composition c be sintered to a theoretical density of at least 90% by pressureless sintering. In another aspect, a method is provided comprising sintering a composition comprising an apatite to a theoretical density of at least 90% by pressureless sintering.

Brief Summary Text (30):
The invention also provides a method involving precipitating crystalline apatite from solution. The crystalline apatite has an average crystall size of less than 250 nm and a BET surface area of at least 40 m.sup.2 /g. The precipitation is carried out under conditions, including temperature, in which, at a temperature at least 20.degree. C. different from the precipitating temperature and under identical conditions othe than temperature, crystalline apatite is precipitated having an average crystallite size of greater than 250 nm and a BET surface area of less t 40 m.sup.2 /g.

Brief Summary Text (31):
The invention also provides a method involving sintering a quantity of apatite powder at a temperature of at least 900.degree. C. while allow apatite phase decomposition of less than 10% in the material.

Brief Summary Text (32):
The invention also provides a composition comprising nanocrystalline apatite that has a theoretical density of at least 90% and an average gr size of less than one micron.

Brief Summary Text (33):
A method of the invention, in another embodiment, involves precipitating apatite from a solvent as an apatite precipitate. Solvent is removed from the apatite precipitate, and the precipitate, particulate apatite is recovered having an average particle size of less than 1 micron.

Brief Summary Text (34):
The invention also provides a method that involves calcining nanocrystalline apatite at a temperature of less than 1000.degree. C. and recovering a nanostructured apatite product having a BET surface area of at least 40 m.sup.2 /g and an average particle size of less than 1 micron.

Brief Summary Text (35):
The invention also includes a method involving sintering apatite in the absence of any sintering additives.

Brief Summary Text (36):
The invention also provides a composition including particulate apatite having a surface area of at least 40 m.sup.2 /g.

Brief Summary Text (37):
A method is provided in accordance with the invention that involves precipitating a particulate apatite from solution having a crystallite size less than 250 nm and a BET surface area of at least 40 m.sup.2 /g under conditions including temperature in which, at a temperature at least 20.degree. different from the precipitating temperature and under identical conditions other than temperature, particulate apatite is precipitat having an average crystallite size of greater than 250 nm and a BET surface area of less than 40 m.sup.2 /g.

Drawing Description Text (2):
FIG. 1 is a series of x-ray diffraction (XRD) patterns of a variety of hydroxyapatite samples involving different preparation treatments;

Drawing Description Text (3):
FIG. 2 is a series of Fourier Transform infrared (PA-FTIR) spectra of nanocrystalline hydroxyapatite as synthesized and after a series of treatment steps;

Drawing Description Text (4):
FIG. 3 is a series of XRD patterns of nanocrystalline hydroxyapatite after a series of treatment steps as in the material identified in FIG. 2;

Drawing Description Text (5):
FIG. 4 is a series of XRD patterns of comparative, conventional, commercially-available hydroxyapatite as received and after a series of treatment steps;

Drawing Description Text (6):
FIG. 5 is an XRD pattern of nanocrystalline hydroxyapatite after calcination; and

Drawing Description Text (7):
FIG. 6 is an PA-FTIR spectrum of the nanocrystalline hydroxyapatite sample for which the XRD pattern is provided in FIG. 5.

Detailed Description Text (3):
Nanocrystalline apatites are provided in accordance with the invention that possess greater reliability, better mechanical properties, and enhanced bioactivity compared to conventional hydroxyapatite with a micron scale microstructure. With minimized flaw sizes, nanocrystalli apatites of the invention are densified without additives at substantially lower temperatures and demonstrate unusual strength and ductility compared to the conventional polycrystalline hydroxyapatite. The nanostructured apatites not only provide superior mechanical properties b also offer the potential for superplastic net-shape forming for inexpensive rapid prototyping. Additionally, apatites can be structurally reinfo by nanocomposite processing involving incorporation of species such as zirconia into apatites.

Detailed Description Text (4):
The invention involves production of nanometer-sized compact resulting from a pressureless sintering process at relatively low sintering temperatures compared to temperatures used in known methods of producing micron-sized hydroxyapatite. A wet chemical approach is used synthesis of preferred compositions leading to the advantages that compositional homogeneity is provided and the method is versatile and ea to control both in terms of the preparative reactions and character of the reaction product. The processing can be tailored for different applications such as densified apatites, coatings, cements, and composites by controlling the morphology, size, reactivity of the precipitated particles, and adjusting their composition.

Detailed Description Text (5):
Apatite compositions of the invention are preferably of nanocrystalline size. Crystal size typically governs bulk properties in an article, with smaller crystal sizes being advantageous for purposes of the invention. Minimization of particle size, by minimizing crystal size, makes densification of particles easier because smaller particles can re-arrange and pack more readily and have a greater driving force for

densification. Accordingly, it is a goal of the invention to provide nanocrystalline apatite powder having an average particle size that approa the average crystal size of the material. The invention involves, in preferred embodiments, a wet chemical approach in which nanocrystals ar precipitated and in which the individual crystals define individual particles, followed by recovery of powder in which the crystals are agglomerated to a minimal extent, and further processing involving densification resulting in materials with useful properties.

Detailed Description Text (6):
The invention provides a method of forming ceramic material that is applicable to a wide variety of materials, including apatitic materials (apatites) such as fluoroapatites and exemplified by hydroxyapatite and carbonate apatite (Type A and Type B). Preferred bioceramics are represented by the general formula M.sub.10.sup.2+ (ZO.sub.y.sup.3-).sub.6 X.sup.2-, where M=Ca, Ba, Sr, Mg, Pb, Cd, etc. where M can b substituted with Na and/or K and consequently the formula can be substituted with an appropriate number of vacancies and/or anions, as kno by one of ordinary skill in the art; ZO.sub.y =PO.sub.4, AsO.sub.4, VO.sub.4, etc. where ZO.sub.y can be substituted with SiO.sub.4, SO.su CO.sub.3, BO.sub.3, etc. to balance a total charge of cations, as known by one of ordinary skill in the art; and X=F.sub.2, (OH).sub.2, Cl.sub Br.sub.2, I.sub.2, O, CO.sub.3 etc. A preferred set of compounds are those that form hexagonally-packed crystals. Calcium-based apatites su as hydroxyapatite are particularly preferred. One set of preferred apatites include calcium phosphate apatites such as Ca.sub.5 (PO.sub.4, CO.sub.3 F).sub.3 R; Ca.sub.5 (PO.sub.4 CO.sub.3 OH)OH; Ca.sub.5 (PO.sub.4).sub.3 Cl; Ca.sub.5 (PO.sub.4).sub.3 F; Ca.sub.5 (PO.sub.4).sub.3 OH; Ca.sub.10 (PO.sub.4).sub.6 CO.sub.3 ; Ca.sub.10 (PO.sub.4).sub.6 O; and non-calcium phosphate apatites such as Ba.sub.5 (PO.sub.4).sub.3 Cl, (Sr,Ce).sub.5 (PO.sub.4).sub.3 OH, (Ce,Ca).sub.5 (PO.sub.4).sub.3 (OH,F), (Y,Ca).sub.5 (PO.sub.4).sub.3 (OH,F), Na.sub.3 Pb.sub.2 (SO.sub.4).sub.3 Cl, Na.sub.3 Ca.sub.2 (SO.sub.4).sub.3 OH, Ca.sub.5 [SiO.sub.4,PO.sub.4,SO.sub.4].sub.3 (C Pb.sub.5 (AsO.sub.4).sub.3 Cl, (Ca,Sr).sub.5 [AsO.sub.4,PO.sub.4].sub.3 OH, Pb.sub.5 (AsO.sub.4).sub.3 Cl, Ca.sub.5 [SiO.sub.4,PO.sub.4,SO.sub.4].sub.3 (F,OH,Cl), Pb.sub.3 Ca.sub.2 (AsO.sub.4).sub.3 Cl, Ca.sub.5 [SiO.sub.4, PO.sub.4,SO.sub.4].sub.3 (OH,F,Cl), Ca.sub.5 (AsO.sub.4).sub.3 OH, Pb.sub.5 (AsO.sub.4).sub.3 Cl, (Ba,Ca,Pb).sub.5 [AsO.sub.4,PO.sub.4].sub.3 Cl, Pb.sub.5 (PO.sub.4).sub.3 Cl, Sr.sub.5 (PO.sub.4).sub.3 (OH,F), Ca.sub.5 (AsO.sub.4).sub.3 F, Ca.sub.5 [AsO.sub.4,PO.sub.4].sub.3 Cl, Pb.sub.5 (VO.sub.4)Cl.

Detailed Description Text (7):
The invention also involves formation of nanocrystalline composites including one or more apatites with other auxiliary additives including ceramics, metals, and alloys. Ceramics preferred for use in composites include alumina, zirconia, titania, silicon carbide, silicon nitrides and other structural ceramics. Metals such as Ti, Al, Ni, W, Fe, Mo, Co, Zr, V, and other structural metals and alloys are useful. Preferably the structural additive also is nanocrystalline. The structural attitude should be selected to strengthen the composite. The auxiliary non-apatite structural component can form a major or minor component, with the overall composite having at least 10% apatite, preferably at least 20% apatite, more preferably at least 50% apatite. Composites can be formed by mixture of two or more component powders, suspension of one o more components in a solution in which one or more other components are dissolved followed by precipitation of one or more solution components, or precipitation from solution of at least two components simultaneously or nearly simultaneously. The latter technique is preferred. Zirconia and alumina are used advantageously in compositions when toughening of a composition is desired. Compositions can be formulated based on mechanical properties desired. For example, if a secondary phase is "pinned" at grain boundaries, that is, forms an intergranular phase, ultra-fine particle size may be maintained by preventing fusion of particles of the first phase, which aids densification an strengthens the material. Secondary phases that form within primary phase grains can deflect cracks, that is, prevent crack propagation withi the primary phase, strengthening the material. Where a composite is formed, it is typically best if the various components are of approximate similar particle size.

Detailed Description Text (14):
The compositions of the invention can be used as coatings. For example, thermal spray coatings, liquid-based coatings, vapor-phase coatings coatings via wet chemical methods, and the like known in the art can benefit from the composition of the invention as the very small particle size results in higher-quality and better-adherent coatings. Porous coatings can be made by admixing an organic species with the bioceramic forming the coating, and burning out the organic material. Similarly, self-assembled surfactants can be used to form very small pores, as described in co-pending, commonly-owned U.S. Pat. application Ser. No. 08/415,695 of Ying, et al., now abandoned, incorporated herein by reference. For larger pore articles, a polymer can be admixed with the bioceramic crystalline powder and burned out after solidification.

Detailed Description Text (15):
The bioceramic material of the invention having very small crystal sizes make it ideal for powders or coatings, and for use with bones. The crystal size of healthy bone is approximately 20-30 nm, and bioceramic material having similar crystal size will be better compatible with bo as a result. In particular, the invention provides compositions including particulate material, preferably apatite, having an average crystal siz less than 250 nm according to preferred embodiments. Preferably, the crystal size is less than 150 nm, more preferably less than 100 nm, mo preferably less than 50 nm, more preferably less than 30 nm, and more preferably still less than 20 nm. In accordance with another set of preferred embodiments, the invention provides bioceramic material having a small average particle size, in particular an average particle size less than 1 .mu.m, preferably having an average particle size of less than 0.5 .mu.m, more preferably still an average particle size of less than 0.25 .mu.m. Any combination of preferred particle size and preferred crystal size can define a preferable combination of the invention, for example an average crystal size of less than 150 nm and an average particle size of less than 1 .mu.m, etc.

Detailed Description Text (16):
The composition of the invention is particulate ceramic material, preferably apatite, that has a high surface area. In one set of embodiments t

surface area is at least 40 m.sup.2 /g, preferably at least 60 m.sup.2 /g, more preferably at least 100 m.sup.2 /g, more preferably still at least 1 m.sup.2 /g. The composition of the invention is particularly robust and resistant to phase decomposition. Apatite compositions of the inventi alone or as part of a composite including an auxiliary structural additive, preferably undergoe apatite phase decomposition of less than 10% when exposed to conditions of at least 1000.degree. C. for at least 2 hours. More preferably a composition undergoes apatite phase decomposition of less than 5%, and more preferably less than 3% under these conditions. In another set of embodiments, the composition undergoes apatite phase decomposition of less than 10% when exposed to conditions of at least 1100.degree. C. for at least 2 hours, preferab less than 5% and more preferably less than 3% under these conditions. In another set of embodiments apatite phase decomposition of less th 10% is realized when the composition is exposed to conditions of at least 1200.degree. C. for at least 2 hours, and apatite phase decompositi is preferably less than 5% and more preferably less than 3% under these conditions. In another set of embodiments, one exposed to condition of at least 1300.degree. C. for at least 2 hours such compositions undergo apatite phase decomposition of less than 10%, preferably less than 5%, and more preferable less than 3%.

Detailed Description Text (17):
The invention provides articles having a dimension of at least 0.5 cm made of any of the above-described or other compositions of the invention. The article preferably is a densified nanocrystalline apatite article where "densified" is defined as having undergone a densificatio step to create a self-supporting particle and, preferably, densified to a theoretical density of at least 75%. The article can be formed into the shape of a prosthesis, or can define at least part of a prosthesis such as an exterior coating on a prosthesis. When used as an exterior coating a prosthesis, the article is at least 0.5 .mu.m thick in at least one region, and the dimension of at least 0.5 cm is a lateral dimension relative to article coated. The theoretical density of articles of the invention preferably is at least 90%, more preferably at least 95%, and more preferab still at least 98%. Porous articles can be provided in accordance with the invention, for example for stimulating bone ingrowth, and where porosity is desired articles having a porosity of at least 20% are preferred, more preferably the porosity is at least 30%, more preferably at le 50%, and more preferably still at least 75%.

Detailed Description Text (19):
The compositions of the invention can be provided as consolidated particulate apatite, where "consolidated" is meant to define a collection o apatite particles that forms a self-supporting structure. Apatite can be consolidated by providing particulate apatite in a press and compressin the apatite to form an article. The consolidated particulate apatite can be dense, or porous.

Detailed Description Text (20):
In all compositions, articles, and methods of the invention, preferred compositions, articles, and products of methods is hydroxyapatite, optionally in combination with an auxiliary structural additive to define a composite article.

Detailed Description Text (21):
In order to produce nanocrystalline apatites having properties tailored for a particular application, a series of processing parameters are provided in accordance with the invention that affect the molecular and structural development and chemistry of apatites, such as aging temperature, aging time, addition rate of reactants (such as addition rate of Ca(NO.sub.3).sub.2 to basic (NH.sub.4).sub.2 HPO.sub.4 solutio hydroxyapatite production), NH.sub.4 OH concentration during chemical precipitation, and precursor concentration. Parameters affecting th agglomeration and densification of ceramic particles such as grinding method, calcination temperature, and sintering temperature also are provided. By reducing crystallite size, ceramics are toughened as the volume fraction of grain boundaries increases allowing grain boundary sliding. Furthermore, by achieving smaller crystallite sizes, defect size is reduced. By minimizing particle size, packing and densification are enhanced.

Detailed Description Text (22):
In one set of embodiments the method in the invention involves precipitating apatite from a solvent by adding a calcium salt to a phosphate source. Suitable calcium salts and phosphate sources would be recognized by those of ordinary skill in the art after reading the present disclosure. In one embodiment apatite is precipitated from a solvent containing a calcium salt in a concentration of less than 1 M, preferably less than 0.5 M, and more preferably from about 0.16 M to about 2.1 M. Preferred methods include precipitating apatite from a solvent containing a calcium salt and phosphate source in a molar ratio of about 10:6. A separate set of embodiments involves mixing a calcium sou and a phosphate source in any way.

Detailed Description Text (24):
pH has been found to be an important parameter in many circumstances, and apatite is preferably precipitated from a solvent at a pH of from about 7 to about 14, more preferably from about 11 to about 13. Apatite crystals are precipitated having a crystal size according to preferred embodiments described above, and precipitated particulate apatite having surface areas as described above, in particular preferably at least 4 m.sup.2 /g, 60 m.sup.2 /g more preferably at least 100 m.sup.2 /g, and more preferably still at least 150 m.sup.2 /g, are recovered. It has also been found that wet grinding the resulting precipitate from the precipitation step of the invention is advantageous.

Detailed Description Text (25):
The apatite product precipitated in accordance with the invention is preferably aged at a temperature of between about -25.degree. C. and ab 100.degree. C., more preferably between about 10.degree. C. and about 50.degree. C., and more preferably still approximately room temperature, i.e. about 20.degree. C. The apatite is preferably aged for at least one minute.

Detailed Description Text (26):
The invention involves calcining nanocrystalline apatite, in a preferred set of embodiments, under a set of conditions that allow recovery of apatite product that is particularly pure and robust as described above. In preferred embodiments the recovered apatite product is of a nature such that it can be sintered at mild conditions of temperature less than 1100.degree. C., yet results in a product having a theoretical density o least 95% and a grain size of less than 225 nanometers. Most preferred are products which can be sintered at a temperature of less than 1000.degree. C. resulting in a product having a theoretical density of at least 98%, and a nanostructured apatite product recovered preferably has an BET surface area of at least 40 m.sup.2 /g and a crystal size of less than 250 nm.

Detailed Description Text (27):
As noted above, the invention involves a sintering technique using compositions of the invention that results in very low decomposition. Pressureless sintering preferably takes place at a temperature of no more than 1100.degree. C. for a period of time of no more than 2 hours, more preferably no more than 1000.degree. C. for this period of time, and more preferably still no more than 900.degree. C. for 2 hours. Apa phase decomposition of less than 10% occurs in this sintering step, preferably decomposition of less than 5%, preferably less than 3%. Sinte can be carried out in the absence of sintering aids. Such additives are known, and are mentioned above. Pressureless sintering is preferred an possible because of the unique nature of the compositions of the invention. In particular, the average crystal size of particulate apatite of the invention is small enough that the composition can be sintered to a theoretical density of at least 90% by pressureless sintering, preferably at least 95%, and more preferably still at least 98% by pressureless sintering, in each case at a grain size preferably of less than 225 nanometers a temperature of no more than 1200.degree. C. in one set of embodiments, more preferably no more than 1100.degree. C., more preferably n more than 1000.degree. C., and more preferably still the pressureless sintering to a theoretical density of 90%, 95%, or preferably 98% is carried out at a temperature of no more than 900.degree. C. The pressureless sintering steps can be carried out to result in a densified apatite product having undergone decomposition of less than 10%, more preferably less than 5% and more preferably still less than 3%.

Detailed Description Text (28):
Another aspect of the invention involved techniques for colloidal and hot pressing of apatites. Hot pressing is a form of pressure-assisted sintering where by a pressure is applied uniaxially to a powder contained within the die during sintering under a vacuum. The pressure-assist sintering allows for more rapid densification and a lower sintering temperature. However, because the hot pressing occurs under a vacuum, t decomposition reaction of hydroxyapatite is favored, necessitating a lower sintering temperature to prevent decomposition. Colloidal pressin (wet pressing) is a process by which a stabilized sol of hydroxyapatite is uniaxially pressed in a die. A stabilized sol of material is defined as suspension of particles which do not undergo sedimentation appreciably over time. Frits within the die allow the solvent to escape as the die pressurized while trapping the solid particles. Once enough solvent is removed to obtain a solid pellet, the pellet is removed and is carefully dried to prevent drying stresses from cracking the pellet. After fully drying the pellet, the pellet is CIPed and undergoes normal pressureless sintering. By avoiding a dry powder phase, colloidal pressing prevents the agglomeration associated with working with a dry powder and benefits from the lubrication effects of the solvent during pressing, which allow the particles in solution to rearrange into the densest packing The present invention provides synthesis conditions for successful hot pressing and colloidal pressing.

Detailed Description Text (29):
As mentioned, all of the compositions and articles of the invention can include an auxiliary structural additive, and methods of the invention involve formation of apatite material including auxiliary structural additive. The auxiliary structural additive can be a metal oxide, preferably selected from among zirconia, titania, and alumina, and/or any combination of these alone or with other known structural additives, defining composite. The auxiliary structural additive can be added in an amount of from about 1 to about 50% by volume, preferably from about 15 t about 35% by volume. The additive can be nanocrystalline to form a "nano/nano" composite. In methods of the invention involving precipitation, apatite can be precipitated from a solvent containing, in suspension, an auxiliary structural additive, or apatite can be provided suspension in a solvent from which is precipitated the auxiliary structural additive or, preferably, the apatite and auxiliary structural additive additives are co-precipitated essentially simultaneously. Nanocrystalline apatite can be calcined in the presence of auxiliary structural additiv and a nanostructured apatite product recovered. Similarly, sintering of the nanocrystalline apatite in the presence of the auxiliary structural additive is advantageous. Alternatively, apatite powder can be independently recovered and auxiliary structural additive independently provi (rather than precipitation from a common solvent or suspension), and admixed and sintered.

Detailed Description Text (30):
Using apatite synthesis via the wet chemistry route provided in the invention, a variety of useful applications are realized. First, nanocrystall apatite powders are provided. Furthermore, since the nanocrystalline apatites of the invention have superior sinterability, they can be easily developed into dental and orthopedic implants requiring densified hydroxyapatite parts. Composites provided in the invention, such as zirconia-toughened apatites possess even better mechanical strength than pure apatites and have the potential as material of choice for load-bearing applications. Also, since densified apatites are provided that are thermally stable up to 1300.degree. C., they can be used in hig temperature applications. The chemical precipitation process of the invention can also be modified to provide a variety of other novel produ such as coatings, cements, nanocrystalline carbonate apatites as artificial bone crystals, and nanocrystalline fluoroapatite for dental applicatio

Detailed Description Text (31):
As mentioned above, the invention also involves the substitution of carbonate for hydroxide in processing resulting in Type A carbonate apa

and substitution of carbonate for phosphate in processing resulting in Type B carbonate apatite. In its broadest sense, the invention according this aspect involves processing conditions, for carbonate apatite, according to the preferred ranges of temperature, pH, aging time, and other parameters listed above as important to the invention in connection with hydroxyapatite. In addition, for the carbonate apatite embodiment, carbonate source, method of carbonate introduction, temperature, aging time, and pH are important, especially for carbonate apatite. Produc made according to these methods also are a part of the invention.

Detailed Description Text (34):
Synthesis and Characterization of Nanocrystalline Hydroxyapatite

Detailed Description Text (35):
A nanocrystalline hydroxyapatite powder was successfully synthesized that allowed pressureless sintering without glassy sintering aids at a remarkably low temperature of 1100.degree. C. for 2 hours or less, resulting in a material that was >98% dense.

Detailed Description Text (36):
A series of experiments were conducted to determine the feasibility of synthesizing nanocrystalline hydroxyapatite and to determine the opti pH, aging temperature, aging time, and heat treatment where the optimal hydroxyapatite is the sample that possesses the highest green and sintered densities. Reagant grade Ca(NO.sub.3).sub.2.4H.sub.2 O and (NH.sub.4).sub.2 HPO.sub.4 were used as starting materials. Aqueous solutions of (NH.sub.4).sub.2 HPO.sub.4 (NHP) and Ca(NO.sub.3).sub.2 (CaN) were prepared such that the Ca:P ratio was 10:6. 0.300 M (NH.sub.4).sub.2 HPO.sub.4 and 0.500 M Ca(NO.sub.3).sub.2 as well as 0.100 M (NH.sub.4).sub.2 HPO.sub.4 and 0.167 M Ca(NO.sub.3).sub.2 were prepared. These solutions were mixed with a magnetic stirrer. The pH of the NH.sub.4).sub.2 HPO.sub.4 aqueous solution was varied by adding concentrated NH.sub.4 OH. 300 ml of a 0.500 M solution of Ca(NO.sub.3).sub.2 was added to 300 ml of 0.30 M aqueous (NH.sub.4).sub.2 HPO.sub.4, or 900 ml of a 0.167 M solution of Ca(NO.sub.3).sub.2 was added to 900 ml of 0.100 M aqueous (NH.sub.4).sub.2 HPO.sub.4 solution at a rate from 2 ml/min to 48 ml/min; the number of moles of precursors was constant in both set of reactions. The combined solution was magnetically stirred for 12 or 100 hours and aged at 0.degree. C., room temperature, or 70.degree. C., The white precipitate was collected by centrifugation at 1500 rpm for 15 minutes. After decanting, the precipitate was redispersed in a distill water and NH.sub.4 OH solution by magnetically stirring for 20 minutes; this procedure was repeated two more times with decreasing amou of NH.sub.4 OH and a fourth and final time with ethanol. The gel was air dried at room temperature for 24 hours and then dried in a 150.deg C. oven for an additional 24 hours. The gel was then finely ground with an alumina mortar and pestle. Instead of air drying the gel, the gel w also wet ground. Wet grinding is a procedure by which a gel is ground in a heated mortar and pestle until the gel becomes a fine powder. Th ground powders we re then heat treated in air at 550.degree. C., 700.degree. C. and 900.degree. C. with a heating rate of 10.degree.C./min, a a dwell time of 2 hours.

Detailed Description Text (38):
The hydroxyapatite powders heat treated at 550.degree. C. in air were sieved and ground to a mesh size of 230. The powders were uniaxially pressed in stainless steel dies at 150 MPa. Pellets were produced using an 8 mm diameter die. From 0.15 g of sample, these compacted pelle were then cold isostatically pressed (CIPed) at 300 MPa in oil for 3 minutes. After CIPing the pellets were sintered in air atmosphere by nor pressureless sintering. Pressureless sintering was done at 1100.degree. C. for 2 hours with a heating rate of 5.degree. C./min. Sintering was a performed at 1000.degree. C., 1100.degree. C., 1200.degree. C., 1300.degree. C. with a heating rate of 5.degree. C./min.

Detailed Description Text (40):
Nano-hydroxyapatite powder calcined at 550.degree. C. were characterized by photoacoustic Fourier-transform infrared spectroscopy (PA-FTIR) on a Biorad Digilab spectrometer and by X-ray powder diffraction (XRD) on a Siemens D5000 diffractometer (45kV-40mA, Cu-K.alpha.). The XRD pattern was analyzed using a Scherrer's analysis of the (002) peak which corresponds to a d-spacing of 3.44 .ANG. determine the XRD crystallite size. The BET surface area and pore size distribution of nano-hydroxyapatite powder after a 550.degree. C. he treatment were evaluated with nitrogen adsorption analysis (Micromeritics ASAP2000). Densities of the green and sintered pellets were measured geometrically and by Archimedes method using water, respectively. The theoretical density was assumed to be 3.16 g/cc. Densifie and sintered HAP pellets were characterized by XRD.

Detailed Description Text (42):
Determination of Optimal Conditions--Calcination, and Comparison With Commercially-Available Hydroxyapatite Powder

Detailed Description Text (43):
One sample of nanocrystalline hydroxyapatite from Example 1 (Trial 2) was heat-treated in air at 550.degree. C., 700.degree. C., and 900.degree. C. for 2 hours in order to investigate the effect of calcination temperature on the microstructure of hydroxyapatite; Trial 2 synthe conditions are presented in Table 1. The XRD patterns of the as-synthesized hydroxyapatite at various calcination temperatures (FIG. 1) indicated that the sample heat treated at 550.degree. C. had better crystallinity than the precursor gel prior to the heat treatment, although the peaks were still quite broad. The heat treatment at 700.degree. C. gave increased crystallinity compared to the sample treated at only 550.degree. C. and was composed of only hydroxyapatite. Even after calcination at 900.degree. C., the sample was found to be composed of only hydroxyapatite. The XRD patterns of the as-received conventional hydroxyapatite powders (Aldrich) (FIG. 1(b)) showed the presence o CaHPO.sub.4.2H.sub.2 O (brushite) and Ca.sub.3 (PO.sub.4).sub.2 (beta-tricalcium phosphate or .beta.-TCP). By 700.degree. C., this mater contained substantial amount of Ca.sub.3 (PO.sub.4).sub.2 while our nanocrystalline material gave only a pure hydroxyapatite phase.

Detailed Description Text (44):
The effect of calcination in air on the molecular structure of the nanocrystalline hydroxyapatite powder was studied with PA-FTIR. The FTI spectrum in FIG. 2 of the nanocrystalline hydroxyapatite powder calcined at 550.degree. C. was similar to that of the as-synthesized hydroxyapatite precursor gel, although the peak at 875 cm.sup.-1 associated with HPO.sub.4.sup.2- was reduced. The PO.sub.4.sup.3- peaks near 1030-1090 cm.sup.-1 and at 560-600 cm-1 also became more well-resolved after calcination indicating that the hydroxyapatite structure became more defined. With increasing temperature, the broad band at 3000-3400 cm.sup.-1 became less prominent as water was removed. T peak intensities of CO.sub.3.sup.2- around 1400 cm.sup.-1 and H.sub.2 O at 1630 cm.sup.-1 were substantially reduced.

Detailed Description Text (45):
The surface areas of nano-hydroxyapatite powder after calcination at various temperatures are summarized in Table 2. Hydroxyapatite calcin at 550.degree. C. has a high BET surface area of 107.5 m.sup.2 /g, compared to 39.5 m.sup.2 /g for the as-received conventional hydroxyapa powder (Aldrich). The increase in calcination temperature decreased the surface area of nano-hydroxyapatite powder. Thus, the optimal calcination temperature for the pure nano-hydroxyapatite powder is 550.degree. C. because phase homogeneity and high surface area are retained while volatiles are removed by this calcination temperature making the powder ideal for compaction.

Detailed Description Text (47):
Determination of Optimal Conditions--Sintering, and Comparison with Commercially-Available Hydroxyapatite Powder

Detailed Description Text (48):
The Trial 2 hydroxyapatite calcined at 550.degree. C. in air was CIPed and sintered at 1000.degree. C., 1100.degree. C., 1200.degree. C. and 1300.degree. C. in air. Conventional hydroxyapatite is known to be stable up to 1360.degree. C. (K. De Groot, C. P. A. T. Klein, J. G. C. Wolker, and J. De Blieck-Hogervorst, "Chemistry of Calcium Phosphate Bioceramics," Handbook of Bioactive Ceramics: Calcium Phospha and Hydroxyapatite Ceramics, Vol 2, pp. 3-15, Edited by T. Yamamuro, L. L. Hench, and J. Wilson, CRC. Press, Boca Raton, 1990). The decomposition reaction is Ca.sub.10 (PO.sub.4).sub.6 (OH).sub.2 .fwdarw.3Ca.sub.3 (PO.sub.4).sub.2 +CaO+H.sub.2 O and begins at 1200.degree. C. (K. Kamiya, T. Yoko, K. Tanaka, Y. Fujiyama, "Growth of Fibrous Hydroxyapatite in Gel System," J. Mater. Sci., 24, 827-832, 1989). It has been reported that even below 1200.degree. C. the loss of OH.sup.- may occur (K. R. Venkatachari, D. Huang, S. P. Ostrander, W. Schulze, and G. C. Stangle, "Preparation of Nanocrystalline Yttria Stabilized Zirconia" J. Mater. Res., 10,756-761, 1995). Th formation of CaO and TCP results in a weakening in mechanical properties and chemical stability. It has been reported that hydroxyapatite w lower Ca/P ratio begins to turn into .beta.-TCP by loss of water at 800.degree. C. (T. Kanazawa, T. Umegaki, and H. Monma, Apatites, New Inorganic Materials, Bull, Ceramic Soc. Jpn., 10, 461-468 (1975)). The temperature of decomposition is known to be dependent on the purit and Ca/P ratio of the powder. The decomposition of hydroxyapatite with a high Ca/P ratio is inhibited even at higher temperatures.

Detailed Description Text (49):
Thus, a superior hydroxyapatite would require excellent compositional homogeneity and could be subjected to a high temperature without decomposition, facilitating densification and maintaining mechanical integrity, and this is provided in accordance with the invention. FIGS. and 4 illustrate the effect of sintering temperature on the XRD patterns of nano-hydroxyapatite powder and a comparative example of conventional hydroxyapatite powder (Aldrich), respectively.

Detailed Description Text (50):
Trial 2 nanocrystalline compact showed only hydroxyapatite peaks with no secondary .beta.-TCP and CaO phases up to 1300.degree. C. On other hand, the XRD results showed that the conventional (Aldrich) compact sintered at 1000.degree. C. has decomposed significantly to .beta.-TCP with some CaO. By 1300.degree. C., the main component was .beta.-TCP with some CaO contained in the .beta.-TCP matrix. Whereas the comparative compact began to transform to .beta.-TCP by 1000.degree. C., the nanocrystalline compact was found to be resista to decomposition even at 1300.degree. C.

Detailed Description Text (53):
The size of particle agglomerates can be reduced by techniques such as wet grinding. Smaller agglomerates allow for ceramic densification a lower sintering temperatures. By using a wet grinding technique, that is grinding the as-synthesized wet gel in a heated mortar until a fine powder is obtained, the size of the agglomerates can be reduced. If the gel is left to dry, capillary pressure begins to build up between the particles as the solvent between the particles is evaporated, squeezing the particles together to form large agglomerates. By wet grinding, the agglomerates are continually broken apart as more surface area is exposed. It is expected that wet ground powder has a higher surface area, a higher green and sintered densities than a dried gel. The green crystallite sizes would be expected to be similar given that the precipitation conditions are identical. The synthesis conditions of the calcined hydroxyapatite powders used to determine the effect of wet grinding are presented in Table 3. XRD crystallite size, BET surface area, green density and bulk density after sintering at 1100.degree. C. are presented Table 4.

Detailed Description Text (54):
Results in Table 4 clearly confirm that wet grinding strongly affect the agglomerate size. The wet ground hydroxyapatite powders possess higher surface area, green density and sintered bulk densities than the dry ground powders. These results suggest that by grinding the gel wh it is still wet, agglomerates size can be reduced thereby enhancing densification. Furthermore, wet grinding the gel does not affect the

crystallinity of the material as shown by the XRD patterns of Trials 1 and 2. The wet and dry ground materials had a similar hydroxyapatite crystallite size. The PA-FTIR spectra showed the presence of OH.sup.-, H.sub.2 O, and PO.sub.4.sup.3- as well as HPO.sub.4.sup.2- and a minor CO.sub.3.sup.2- peak. Since wet grinding did not affect the crystallinity of the material but did significantly reduce agglomeration, it should be utilized in the processing of the hydroxyapatite precursor gel.

Detailed Description Text (58):
As shown in Table 6, the calcined powders reacted and aged at 70.degree. C. had larger crystallites than the powders reacted and aged at roo temperature and 0.degree. C. Since room temperature processing readily yields high green and sintered densities, 25.degree. C. is the preferr reaction and aging temperature for the chemical precipitation of hydroxyapatite.

Detailed Description Text (61):
The crystallinity and structural development of hydroxyapatite can be affected by varying the aging time. By increasing the aging time, the hydroxyapatite precipitate undergoes recrystallization. As a result, occluded impurities are removed and crystal strain is reduced as free ener of the crystal decreases, while the crystal structure becomes perfected and the exposed area is decreased. Needle-like and rod-like structures redissolve and are recrystallized in more orderly morphologies such as spheres with the shapes of the primary particles approaching a homogeneous distribution. This phenomena can be also accompanied with a decrease in surface area. Furthermore, longer aging times ensur that the reagents are fully reacted and precipitate out of the solution. The synthesis conditions of the hydroxyapatite gels used to determine th effect of aging time are presented in Table 7.

Detailed Description Text (62):
The XRD patterns of Trials 5, 6, 7, and 8 agree with the JCPDS hydroxyapatite file (9-0432), and no other phases were observed. Trial 8 possessed a smaller XRD crystallite size than Trials 7 while similar grain sizes were noted for Trials 5 and 6. These results indicate that hydroxyapatite aged for 100 hours had a noticeably smaller average crystallite size than hydroxyapatite aged for 12 hours in hydroxyapatite prepared with the lower precursor concentration. Although FTIR spectra of Trials 5, 6, 7, and 8 possessed peaks characteristic of hydroxyapatite, the HPO.sub.4.sup.2- peak at 875 cm.sup.-1 and the peaks of PO.sub.4.sup.3- at 1030-1090 cm.sup.-1 and 560-600 cm.sup. were reduced in intensity and were broadened for the sample aged for 100 hours. The XRD patterns and the FTIR spectra indicated that the hydroxyapatite aged for 100 hours underwent significant dissolution and reprecipitation so that the crystallite size of the reprecipitated hydroxyapatite was smaller than that of the originally precipitated hydroxyapatite. Alternatively, amorphous calcium phosphate may have nucleated into small crystallites during long aging times reducing the average crystallite size.

Detailed Description Text (63):
Significant differences in the effect of aging time are observed for the hydroxyapatite synthesized using high and low precursor concentratio In both cases, an increase in surface area is observed as aging time is increased, though a decrease in surface area is expected with longer ag times as predicted by Ostwald ripening. Instead of an Ostwald ripening phenomenon, there is a conversion from a low surface area amorpho calcium phosphate to a higher surface area crystalline hydroxyapatite; this interpretation is consistent with the decrease in XRD crystallite si as aging time is increased. The hydroxyapatite synthesized using 0.500 M Ca(NO.sub.3).sub.2 and 0.300 M (NH.sub.4).sub.2 HPO.sub.4 precursor concentrations aged for 12 hours (Trial 5) resulted in a higher sintered density than that aged for 100 hours (Trial 6). However, for hydroxyapatite synthesized using 0.167 M Ca(NO.sub.3).sub.2 and 0.100 M (NH.sub.4).sub.2 HPO.sub.4 precursor concentrations, aging fo 100 hours (Trial 8) resulted in a higher sintered density than aging for 12 hours (Trial 7). These results suggest that particle morphology of t originally precipitated hydroxyapatite synthesized at high precursor concentrations (Trial 5) favors densification, while the particle morpholo of the reprecipitated hydroxyapatite synthesized at low precursor concentrations (Trial 8) favors densification.

Detailed Description Text (66):
pH can affect chemical precipitation by altering the solubility of the precipitate; the solubility of hydroxyapatite decreases as pH increases. A result, nucleation would be favored decreasing crystallite size. Furthermore, different pH's affect agglomeration by inducing a surface charge the particles in solution. Similar surface charges in the solution of the particles repel each other reducing agglomeration in the solution. However, the same polar solvents that prevented agglomeration during precipitation introduce surface hydroxyl groups onto ceramic particle during the drying process. As the ceramic gel dries, the surface hydroxyl groups promote agglomeration of particles. It is therefore desirable use a nonpolar solvent, to wash the gel in order to remove the surface hydroxyl groups. Finally, the different pHs during the chemical precipitation are expected to affect crystal morphology, and the morphology becomes increasingly rod-like with increasing pH. Tanahashi et reported that the solution pH greatly influenced the growth rate and morphology of hydroxyapatite and that fibrous hydroxyapatite could be prepared at high pH. Hydroxyapatite synthesized through hydrothermal treatment at a pH of 11 to 12 also resulted in nanometer-sized rod-lik crystals. However, the addition of glycerin during the synthesis confounded the relationship between high pH and the synthesis of rod-like hydroxyapatite, with the effect of additives on the synthesis of rod-like hydroxyapatite. The synthesis conditions of the calcined hydroxyapat powders used to determine the effect of NH.sub.4 OH are presented in Table 9.

Detailed Description Text (67):
The XRD patterns show that all of the calcined hydroxyapatite samples, except for Trial 13, have good crystallinity and a pure hydroxyapati phase. The peaks of the FTIR spectra were also consistent with hydroxyapatite. Trials 9, 5, and 10 correspond to 10 ml, 30 ml, and 100 ml o NH.sub.4 OH at high precursor concentrations. The XRD results of Trials 9 and 5 suggest that the addition of more NH.sub.4 OH gives rise smaller XRD crystallites, which is consistent with the effect of increased pH which decreases solubility, favoring nucleation. However, the X

crystallite size of Trial 10 is larger than Trial 5. This phenomenon can be explained by examining Trials 11,12, and 13 which correspond to ml, 90 ml, and 300 ml of NH.sub.4 OH at low precursor concentrations. The XRD crystallite sizes of Trials 11 and 12 decrease as pH is increased. Similar to Trial 10, Trial 13 deviates from the trend established by Trials 11 and 12. Instead of the anticipated further decrease in XRD crystallite size, as-synthesized Trial 13 is not hydroxyapatite but a combination of monetite (CaHPO.sub.4) and brushite (CaHPO.sub.4.2H.sub.2 O) Trial 10 may occur in a similar metastable state as Trial 13, though not as pronounced because of its shorter agin time and higher precursor concentrations. Thus, the possible presence of monetite and brushite during the synthesis of Trial 10 may give rise the deviation in the crystallite size. Furthermore, samples prepared under similar conditions as Trial 13 have resulted in hydroxyapatite, confirming the metastability of this region.

Detailed Description Text (68):
Trial 9, the hydroxyapatite derived with 10 ml of NH.sub.4 OH, resulted in the highest surface area and the highest % theoretical sintered bu density under a high precursor concentration synthesis. A low pH at high precursor concentrations produces a particle morphology and distribution favorable towards densification since the addition of NH.sub.4 OH is known to affect particle morphology. Conversely, at low precursor concentrations, the highest surface area and highest % theoretical sintered bulk density occurred at an intermediate pH, indicating this amount of NH.sub.4 OH resulted in a particle morphology and distribution favorable toward densification.

Detailed Description Text (71):
By varying the precursor addition rate, nucleation and crystal growth rates can be controlled. Rapid addition of precursors results in localize high concentrations of precursors, exceeding the solubility of hydroxyapatite in those regions, which favors nucleation and formation of sma particles. However, rapid addition is also expected to result in a nonuniform particle morphology and distribution. Conversely, slow addition precursors results in a more homogenous mixture of reactants favoring crystal growth and formation of larger particles. Furthermore, slow addition of precursors is anticipated to result in a uniform particle morphology and distribution. Thus, relatively few nuclei will be formed b adding Ca(NO.sub.3).sub.2 slowly; crystal growth removes the precursors as fast as it is added. Adding Ca(NO.sub.3).sub.2 quickly yields m and smaller particles. The synthesis conditions of the experiment investigating the effect of addition rate are presented in Table 11.

Detailed Description Text (72):
The XRD patterns of Trials 9, 14, 15, and 12 corresponded to the JCPDS hydroxyapatite file (9-0432) and no other phases were found. All FTIR spectra possess peaks characteristic of nanocrystalline hydroxyapatite. Trials 9 and 15 possessed a larger XRD crystallite size and a higher BET surface area than Trials 14 and 12, respectively, and gave rise to higher sintered densities. The larger XRD crystallite sizes of T 9 and 12 compared to 14 and 12 suggest that a slower addition rate favors crystal growth, as anticipated. In addition, by using a slow additio obtain a more uniform particle morphology and distribution, the final sintered bulk densities were enhanced. These effects were significant f Trials 9 and 14, but addition rate did not play a dominant role in Trials 15 and 12. The lesser role of addition rate at low precursor concentrations can be attributed to the difference in molar flow rates. The difference in molar rates between Trials 15 and 12 is 7.5.times.10.sup.-3 moles/min whereas the difference in molar flow rates between Trials 9 and 14 is 7.4.times.10.sup.-2 moles/min. These results confirm that crystallite size depends on the rate of addition with slower rates of addition resulting in larger crystallites, but to observe this effect at low precursor concentrations, a much higher flow rate should be used. To obtain a densified nanocrystalline hydroxyapatite ceramic, Ca(NO.sub.3).sub.2 should be added slowly to the basic (NH.sub.4).sub.2 HPO.sub.4 solution.

Detailed Description Text (75):
By varying the precursor concentration, the synthesis of nanocrystalline hydroxyapatite can be further controlled by affecting the kinetics of hydroxyapatite synthesis. By reducing the precursor concentration, the kinetics of the reaction are slowed. The synthesis conditions of the hydroxyapatite gels used to determine the effect of precursor concentration are presented in Table 13.

Detailed Description Text (76):
The XRD patterns of Trials 9, 17, and 15 correspond to hydroxyapatite while the XRD pattern of Trial 16 corresponds to monetite (CaPO.su OH). The FTIR spectra of Trials 9, 17, and 15 also showed the characteristic hydroxyapatite nanocrystalline peaks. By reducing the precurso concentration in Trial 9 to the precursor concentration of Trial 16, hydroxyapatite synthesis enters an intermediate state where monetite is th product. In Table 8, "Effect of Aging Time," Trials 7 and 8 were both found to be hydroxyapatite regardless of aging time, but unlike Trial 1 Trials 7 and 8 were synthesized under a higher pH. Tables 15 and 16 present the synthesis conditions and results proving that Trial 16 is an intermediate state, observable because of the shorter aging time, low precursor concentration and low pH; under the same conditions as Tria 16, except with longer aging times, Trial 11 was determined to be hydroxyapatite. Thus, the effect of lowering precursor concentration at the synthesis conditions of Trials 9 and 16 is to slow the kinetics of the reaction.

Detailed Description Text (78):
Two synthesis conditions, Trial 9 and 15, were determined to give rise to the optimal hydroxyapatite powders as assessed by % theoretical sintered bulk density. Trial 15 possessed the highest pressurelessly sintered bulk density of all trials investigated. The 95.6% theoretical sinte bulk density was obtained using a low precursor concentration, 100 hour aging time, an aging temperature of 25.degree. C., 3 ml/min Ca(NO.sub.3).sub.2 addition rate, 90 ml of NH.sub.4 OH, and wet grinding. A high theoretical density of 94.3% was obtained using the synthesis conditions of Trial 9: high precursor concentration, 12 hour aging time, an aging temperature of 25.degree. C., 2 ml/min addition r 10 ml of NH.sub.4 OH, and wet grinding. Thus, optimal conditions were determined for the precursor concentrations investigated.

Detailed Description Text (80):
Nanocrystalline hydroxyapatite was synthesized successfully by chemical precipitation. The effects of NH.sub.4 OH amount, aging time, agi temperature, grinding method, precursor concentration, and Ca(NO.sub.3).sub.2 addition rate on the crystallite size, agglomeration, morphology, crystallinity and the molecular structure were examined. By identifying the important processing parameters and the method by which they can be controlled, the crystallite size can be reduced to enhance the mechanical properties of bulk hydroxyapatite. Furthermore, using the parameters to reduce agglomeration, to control the particle morphology and size distribution, and to control the chemical reactivity the particles, full densification can be achieved at lower sintering temperatures. The XRD patterns of the nano-hydroxyapatite precursor gel were in good agreement with the JCPDS hydroxyapatite file (9-432); the peaks were substantially broadened due to the nanocrystalline natur of hydroxyapatite. The grinding method affected the surface area and the state of agglomeration with wet grinding being favored. Reaction a aging temperatures during precipitation affected the crystal growth rate with room temperature favored. Aging time affected the conversion o the precipitate into a crystalline hydroxyapatite, the crystallite size, and the particle morphology and size distribution. Short aging times were preferred by high precursor concentrations and long aging times were preferred by low precursor concentrations. Amount of NH.sub.4 OH affected the solubility of hydroxyapatite and the particle morphology and size distribution. Low NH.sub.4 OH amounts were preferred at hig precursor concentrations favored low NH.sub.4 OH amounts while intermediate NH.sub.4 OH amounts were preferred at low precursor concentrations. Precursor addition rate affected the nucleation and crystal growth rates and particle morphology. Slow addition rates were preferred at both high and low precursor concentrations. Precursor concentration affected the rate of reaction of hydroxyapatite. Optimal conditions were determined for both precursor concentrations. The nano-hydroxyapatite precursor gel heat treated at 550.degree. C. gave an ultrafine grain size of 40 nm by TEM observation. This high-purity nano-hydroxyapatite also had higher B.E.T. surface areas than samples h treated to 700.degree. C. or 900.degree. C. and was used to prepare compacts for pressureless sintering. The nano-hydroxyapatite compact h superior sinterability when compared to conventional hydroxyapatite. The highly densified hydroxyapatite was obtained by pressureless sintering at 1100.degree. C. Also, the dense compacts derived from nanocrystalline hydroxyapatite demonstrated excellent resistance to high-temperature decomposition, compared to the conventional hydroxyapatite. This should give rise to superior properties in bioceramic applications. The nano-hydroxyapatite synthesized in this study was resistant to thermal decomposition into .beta.-TCP and CaO up to 1300.degree. C.

Detailed Description Text (82):
Colloidal and Hot Pressing of Nanocrystalline Hydroxyapatite

Detailed Description Text (83):
By only controlling the synthesis parameters without any subsequent powder processing, 96% theoretical bulk density was obtained, indicati the superiority of this nanocrystalline hydroxyapatite powder. To further illustrate the improvements of the nanocrystalline hydroxyapatite an its processing over the conventional hydroxyapatite and conventional processing and to exceed the 96% theoretical bulk density obtained fro pressureless sintering, the nanocrystalline powders were densified by colloidal and hot pressing.

Detailed Description Text (85):
From the results presented in Table 18, hot pressing is observed to have a dramatic impact on the sintering of the hydroxyapatite powder. Ho pressing increased the % theoretical bulk density of the powder from Trial 9, one of the optimal conditions determined in the previous sectio to 98.5% and enabled Trial 19 to achieve 99% theoretical density. The pellets of Trial 9 and 19 possessed a glassy finish and were slightly translucent. The .beta.-TCP decomposition products, barely detectable by XRD, were found in the XRD patterns of the hot pressed powders from Trials 9 and 19. Furthermore, the grain sizes of the sintered pellets were found to be less than 225 nm by SEM, indicating that an ultraf microstructure was present after the sintering process. Remarkably, even with a powder with poor pressureless sintering characteristics such that of Trial 18, the bulk density can be increased from 2.14 g/cc to 3.05 g/cc through hot pressing. Though this sample decomposed significantly into .beta.-TCP, this pellet was pore-free as indicated by the transparency of the pellet. The operating conditions presented for h pressing provide an upper limit for sintering temperature and a lower limit for the applied pressure because of the slight decomposition detec in the XRD patterns. Observations indicate that densification stops before 1000.degree. C., and that 900.degree. C. or 800.degree. C. may be preferred sintering temperature. By hot pressing, the sintering temperature can be reduced by 200.degree. C. or 300.degree. C. Increasing the applied pressure is also anticipated to facilitates the sintering process. The most dramatic results from hot pressing are associated with a less crystalline and a more amorphous hydroxyapatite starting powder. Hot pressing seems to favor powders synthesized under either low temperature or low precursor concentration conditions. The results from hot pressing are a further demonstration of the superiority of the nanocrystalline hydroxyapatite powder; without any special powder processing, full densification of hydroxyapatite can be achieved.

Detailed Description Text (87):
The sample (Trial 20) prepared by colloidal pressing was synthesized under the similar conditions as Trial 15. The as-synthesized hydroxyapatite gel, instead of rinsing and centrifuging with ethanol in the last two washing steps, was washed with water. A slurry was prepared, and this slurry was colloidally pressed. After careful drying, the pellet was CIPed to 300 MPa and sintered to 1100.degree. C. for 2 hours at 5.degree. C./min. A highly translucent pellet was obtained with a 95.8% theoretical density. However, slight decomposition was detected in the XRD patterns. These data do strongly suggest that the hydroxyapatite prepared by the method described in previous section i well suited to colloidal pressing as indicated by the translucent pellet. A mild hydrothermal treatment of the precipitate prior to colloidal pressing may improve sintering by increasing the crystallinity of the material and by reducing the reactivity of the as-synthesized gel; the hydroxyapatite phase will be more stable and decomposition will be reduced. Furthermore, by controlling the pH and ionic strength of the sl (e.g. by the addition of NH.sub.4 NO.sub.3), the state of agglomeration and particle morphology can be controlled to enhance densification.

Detailed Description Text (89):
Synthesis and Characterization of Hydroxyapatite-Zirconia Composites

Detailed Description Text (90):
A composite including an apatite and a structural additive was prepared, with the additive selected to enhance the mechanical properties. To further strengthen hydroxyapatite and to maintain the nanocrystallinity after sintering, the addition of a secondary component is proposed. M types of hydroxyapatite composites have been developed to take advantage of both the properties of hydroxyapatite and of the secondary phases. Hydroxyapatite-polymer composites have been developed to improve upon the mechanical reliability of conventional hydroxyapatite Hydroxyapatite has also been used as the reinforcing phase in glass-hydroxyapatite composites. Hydroxyapatite composites formed with ano secondary ceramic phase such as alumina or zirconia have been shown to significantly improve the mechanical properties of hydroxyapatite. The hydroxyapatite-alumina composites required complex processing such as glass encapsulated hot isostatic pressing. Significant improvements in mechanical properties were observed when vol % alumina in the composite increased above 50%. However, as the volume of alumina is increased, the bioactivity of the composite decreases. The mechanical properties of the hydroxyapatite-zirconia composites are expected to match or exceed the hydroxyapatite-alumina composites while using a smaller volume % of zirconia. This is because zirconia ha more mechanisms by which it can provide mechanical reinforcement than alumina. Zirconia dispersiods can toughen the hydroxyapatite mat by a transformation toughening mechanism as well as crack deflection. By using nanocrystalline materials processing, the mechanical proper can be further enhanced. The zirconia dispersion can then be used to "pin" the hydroxyapatite grains suppressing grain growth during calcination and sintering to preserve nanometer-sized crystallites.

Detailed Description Text (91):
In trying to develop a composite with the optimal mechanical properties, the effects of the grain sizes of the hydroxyapatite and zirconia, dop concentration, milling time, and milling intensity were investigated. Nanocrystalline hydroxyapatite and zirconia were synthesized by chemic precipitation. Through the previous studies on the synthesis and characterization of hydroxyapatite, the processing parameters can be contro to obtain a specified grain size and particle morphology and sintered density.

Detailed Description Text (92):
Synthesis of Nanocrystalline Hydroxyapatite

Detailed Description Text (97):
In these series of experiments, composites formed from conventional hydroxyapatite (Aldrich), conventional zirconia (Toso), nanocrystallin hydroxyapatite, and nanocrystalline zirconia heat treated at 550.degree. C. were investigated. The composite was formed by dry milling the hydroxyapatite with 10 vol % of zirconia for 24 hours, CIPing at 300 MPa for 3 minutes, pressureless sintering for 2 hours in air at sintering temperatures of 1100.degree. C., 1200.degree. C., and 1300.degree. C. This dry ball milling ensured good mixing and contact between the tw components without the transformations that might occur by high-energy ball milling. The XRD patterns of the nanocrystalline Y.sub.2 O.su -doped ZrO.sub.2 indicated the presence of zirconia as 12 nm crystallites. A PA-FTIR spectrum indicated the presence of Zr-O-Zr, H.sub.2 and ZrOH peaks. The calcined nanocrystalline Y.sub.2 O.sub.3 -doped ZrO.sub.2 possessed a BET surface area of 140 m.sup.2 /g and an average pore size of 9 nm. After calcination at 550.degree. C., the nanocrystalline hydroxyapatite had a XRD crystallite size of 32 nm and a BET surface area of 66.8 m.sup.2 /g.

Detailed Description Text (98):
The XRD patterns of the sintered nano-hydroxyapatite/nano-zirconia composite indicated that the composite was thermally stable up to 1200.degree. C., and that significant phase transformation of hydroxyapatite and zirconia into tricalcium phosphate and monoclinic zirconia, respectively, occurred at 1300.degree. C. When comparing the sinterability of nano-hydroxyapatite and zirconia reinforced hydroxyapatite, t composite required a higher sintering temperature of 1200.degree. C. to achieve full densification while the pure nano-hydroxyapatite requir 1100.degree. C. to achieve full densification. The nanocrystalline composite possessed better sinterability than any composite containing a conventional hydroxyapatite and/or ZrO.sub.2 powder. By 1200.degree. C., the nano-hydroxyapatite/nano-zirconia composite attained 98% theoretical density of hydroxyapatite while nano-hydroxyapatite/zirconia (Toso) achieved less than 70% theoretical density by 1300.degree.

Detailed Description Text (99):
TEM micrographs indicated that there were no glassy phases at the grain boundaries showing that the nanocomposite achieved good densification without the precipitation of undesirable secondary phases. Zirconia grains were intragranularly dispersed within the hydroxyapatite matrix. With smaller grain sizes, a more mechanically robust material is obtained. The pure nanocrystalline hydroxyapatite possessed a compressive strength of 745 MPa while the conventional micron-sized hydroxyapatite possessed a compressive strength of 150 MPa. Further reinforcement of the nanocrystalline hydroxyapatite with a secondary dispersoid of nanocrystalline zirconia resulted in an even higher compressive strength of 1020 MPa. This improvement in compressive strength is believed to be due to the intragranular toughening o the nanocrystalline hydroxyapatite matrix by the nano-ZrO.sub.2 dispersoids.

Detailed Description Text (100):
Another method for the synthesis of nanocrystalline hydroxyapatite yields an improved nanocomposite with an even higher compressive strength, a lower sintering temperature and greater thermal stability. The method of producing the composite uses ajar mill to disperse the

zirconia into the hydroxyapatite. Recent experiments suggests that better mixing and contacting between the zirconia and hydroxyapatite can achieved by co-precipitation, or by dispersing zirconia particles during either the chemical precipitation or the aging of the nanocrystalline hydroxyapatite.

Detailed Description Text (101):
The proof of concept and initial studies of the synthesis of hydroxyapatite/zirconia nanocomposite used an earlier method for the synthesis o nanocrystalline hydroxyapatite. By using the recently optimized method for the synthesis of nanocrystalline hydroxyapatite (Trial 9 or 15), a improved nanocomposite with an even higher compressive strength, a lower sintering temperature and greater thermal stability may be produced. The method of producing the composite reported above used a jar mill to disperse the zirconia into the hydroxyapatite. Recent experiments suggest that better mixing and contacting between the zirconia and hydroxyapatite can be achieved by dispersing zirconia partic during either the chemical precipitation or the aging of the nanocrystalline hydroxyapatite.

Detailed Description Text (103):
Synthesis and Characterization of Nanocrystalline Carbonate Hydroxyapatite

Detailed Description Text (104):
Since the mineral phase of human bone has recently been identified as carbonate apatite, not hydroxyapatite.sup.7, a nanocrystalline carbona apatite can be used as a reactive layer on a bioceramic to enhance bioactivity for bone growth on the surfaces of the implant. Because the po mechanical properties of carbonate apatite prevent it from being used as a structural material, the focus of this work will be the synthesis and characterization of nanocrystalline carbonate apatite powder. With the ability to synthesize a high surface area carbonate apatite powder, the bioactivity of artificial bone crystals can be controlled.

Detailed Description Text (105):
To further illustrate the versatility of the preparative technique developed for synthesis of hydroxyapatite, the chemical precipitation process which nanocrystalline hydroxyapatite is synthesized was modified to derive nanocrystalline carbonate apatite, Ca.sub.10 (PO.sub.4).sub.6 CO.sub.3 (Type A where the CO.sub.3.sup.2- occupies the monovalent anionic (OH.sup.-) sites) or Ca.sub.10-x (PO.sub.4).sub.6-2x (CO.sub.3).sub.2x (OH).sub.2(1-x) (Type B where the CO.sub.3.sup.2- occupies the trivalent anionic (PO.sub.4.sup.3-) sites). Type A carbonate apatite is a well-defined class of compounds normally synthesized at elevated temperatures. In contrast, Type B carbonate apatite poorly defined class of compounds typically synthesized at low temperatures under aqueous conditions. Carbonate apatite can be generated b either saturating the reaction solution with carbon dioxide or by adding another carbonate source such as sodium bicarbonate or ammonium bicarbonate, followed by a hydrothermal treatment, in an attempt to stabilize the carbonate ion in the precipitate.

Detailed Description Text (106):
Synthesis of Nanocrystalline Carbonate Apatite

Detailed Description Text (109):
The synthesis of hydroxyapatite is known to undergo an induction period. Prior to hydroxyapatite formation, the precipitate is thought to convert from an amorphous calcium phosphate to an octacalcium phosphate and then to hydroxyapatite. Furthermore, the induction period increases with increasing pH. By synthesizing the hydroxyapatite at a low pH, higher solubility of hydroxyapatite is anticipated to aid the incorporation of the carbonate ion. In this initial study, the effect of carbonate substitution during pre- and post-HAP formation, the effect of varying the Ca/P ratio, and the effect of aqueous aging versus hydrothermal treatment were examined. In all samples, a mixed phase of hydroxyapatite, Type A and Type B carbonate apatite was detected. Introducing CO.sub.2 immediately after the addition of Ca(NO.sub.3).su was found to minimize the formation of CaCO.sub.3, as determined by the XRD patterns and FTIR spectra. If CO.sub.2 was added 6 hours a Ca(NO.sub.3).sub.2 addition was completed, significant CaCO.sub.3 formed because more calcium cations were in solution as a result of the reprecipitation process, while calcium was bound in the precipitate immediately after Ca(NO.sub.3).sub.2 addition. In both aqueous aging an hydrothermal treatment, CaCO.sub.3 was detected in the XRD patterns when [(NH.sub.4).sub.2 HPO.sub.4]<0.224 M. For aqueously aged samples, both Type A and Type B carbonate apatites were detected in FTIR spectra. 879 cm.sup.-1 is assigned to Type A carbonate apatite, 873 cm.sup.-1 is assigned to Type B carbonate apatite. Type A is favored over Type B for aqueously aged samples when [(NH.sub.4).sub.2 HPO.sub.4]=0.3 M. For this sample, the XRD crystallite size was determined to be 25 nm. This is considerably smaller than the XRD crystallite size determined from hydroxyapatite synthesis which strongly suggests that the presence of the carbonate ions restricts crystal gro CaCO.sub.3 became the dominant phase for aqueously aged samples when [(NH.sub.4).sub.2 HPO.sub.4]<0.224 M. For hydrothermally ag samples, both Type A and Type B carbonate apatites were detected in the FTIR spectra but the relative intensity of the Type A and Type B peaks suggests that hydrothermal treatment is more selective towards Type A carbonate apatite formation. Hydrothermal treatment stabilized the apatite phase with CaCO.sub.3 becoming the dominant phase when [(NH.sub.4).sub.2 HPO.sub.4]<0.075 M. In a subsequent experimen carbonate apatite was synthesized under the following conditions: (1) 300 ml 0.5 M Ca(NO.sub.3).sub.2, (2) 300 ml 0.3 M (NH.sub.4).sub.2 HPO.sub.4, (3) 10 ml NH.sub.4 OH, (4) 80.degree. C. reaction and aging temperature, (5) 3 ml/min Ca(NO.sub.3).sub.2, and (6) immediate introduction of CO.sub.2 after Ca(NO.sub.3).sub.2 was added at 3 ml/min. The XRD pattern was identified as an apatite, with the FTIR spec detecting Type A and Type B with Type A slightly favored. The XRD crystallite size for this sample was 65 nm, also considerably smaller t sizes measured for hydroxyapatite synthesized at similar conditions. These results suggest that Type B will be favored when synthesized at temperatures below 25.degree. C. Furthermore, the introduction of carbonate into the apatite structure may be more carefully controlled by using NH.sub.4 HCO.sub.3 instead of CO.sub.2(g). The surface areas for nanocrystalline carbonate apatite is expected to be similar to or

greater than the surface areas of nanocrystalline hydroxyapatite synthesized under similar conditions.

Detailed Description Text (110):
This example illustrates the versatility of the process developed for synthesizing nanocrystalline hydroxyapatite and the benefits of carefully controlling the process parameters. By introducing a carbonate source and controlling the processing parameters, a nanocrystalline carbonate apatite, both Type A and Type B, was synthesized. Through further refinement, Type A and Type B carbonate apatite can be selectively synthesized, and the degree of substitution of carbonate ions for the phosphate ions in Type B carbonate apatite can be controlled. Important parameters will be reaction and aging temperatures, carbonate source, method of carbonate introduction, precursor concentrations, aging tim and pH.

Detailed Description Text (112):
The above examples demonstrate superior processes and products resulting from densifications of nanocrystalline hydroxyapatite. The grain sizes of calcined samples varied from 30 nm to 100 nm depending how pH, aging time, reaction and aging temperature, Ca(NO.sub.3).sub.2 addition rate, precursor concentration, and grinding method were controlled, while the grain sizes of conventional hydroxyapatite were on a micron scale. For example, the surface area of one sample of the invention after calcination at 550.degree. C. is 159.5 m.sup.2 /g while the conventional sample after calcination at 550.degree. C. has a very small surface area of 5.4 m.sup.2 /g. The sample of the invention retained phase uniformity after calcination at 550.degree. C., but the conventional sample began to transform into tricalcium phosphate at 550.degree with substantial conversion to tricalcium phosphate and calcia by 700.degree. C. In a sample of the invention 96% of the theoretical density obtained at a low sintering temperature of 1100.degree. C. by pressureless sintering for nanocrystalline hydroxyapatite which was stable up t 1300.degree. C. However, the conventional sample achieved only 70% of the theoretical density at 1200.degree. C. with decomposition into tri-calcium phosphate. Furthermore, the densified conventional sample contained large pores and microcracks. Our nanocrystalline hydroxyapatite has high purity and phase homogeneity as well as superior sinterability compared to the conventionally prepared hydroxyapa When our nanocrystalline hydroxyapatite was sintered using either colloidal or hot pressing, 99% theoretical bulk density with a grain size o less than 250 nm can be obtained. Dense nanocrystalline hydroxyapatite compacts further possessed a compressive strength as high as 745 M while the conventional micron-sized hydroxyapatite compacts from a similar pressureless sintering treatment possessed a compressive streng of 150 MPa. Additionally, further reinforcement of the hydroxyapatite can be accomplished by introducing a secondary dispersoid such as zirconia which would greatly improve the toughness and chemical stability of hydroxyapatite by pinning the mobility of any intergranular an intragranular defects. A dense composite of nanocrystalline hydroxyapatite and 10 wt % nanocrystalline 3 mol % Y.sub.2 O.sub.3 -doped ZrO.sub.2 possessed an even higher compressive strength of 1020 MPa. With more complete characterization, the densified nanocrystalline hydroxyapatite and hydroxyapatite-zirconia composites can easily be developed into dental and orthopedic weight-bearing implants. Furthermore, the processing of nanocrystalline hydroxyapatite can be adapted to synthesize a nanocrystalline carbonate apatite illustrating th versatility of our process. This process can also be used to selectively synthesize Type A and Type B carbonate apatite as well as to control t degree of substitution of the carbonate ion into the apatite structure.

Detailed Description Paragraph Table (2):
TABLE 2 ______________________________________ XRD Crystallite Size and BET Surface Area of Hydroxyapatite from TEM Observation and XRD Analysis Calcination Temperature XRD Crystallite Size BET Surface Area (.degree. C.) (nm) (m.sup.2 /g) ______________________________________ as-synthesized 40.0 226.6 550 40.0 107.5 700 75 42.5 900 >100 9.3 Aldrich (as-received) 9 39.5 ______________________________________

Other Reference Publication (5):
J.D. deBruijn et al., "Biological Responses to Calcium Phosphate Ceramics", Bone-Bonding--Reed Healthcare Communications, Ducheyne, Kokubo & Van Blitterswijk, Eds., pp. 57-72, 1992, no month.

Other Reference Publication (7):
M. Jarcho, et al., "Hydroxylapatite Synthesis and Characterization in Dense Polycrystalline Form", J. of Materials Science, 11, pp. 2027-203 (1976), no month.

Other Reference Publication (8):
M. Akao et al., "Mechanical Properties of Sintered Hydroxyapatite for Prosthetic Applications", J. of Materials Science, 16, pp. 809-812 (1981), no month.

CLAIMS:

1. A composition, comprising particulate apatite having an average apatite crystal size of less than 100 nm, wherein the crystal is spherical.

2. The composition of claim 1 comprising particulate apatite having an average apatite crystal size of less than 50 nm.

3. The composition of claim 1 comprising particulate apatite having an average apatite crystal size of less than 30 nm.

4. The composition of claim 1 comprising particulate apatite having an average apatite crystal size of less than 20 nm.

5. A composition as in claim 1 wherein the particulate apatite is densified.

6. The composition of claim 1 comprising apatite having an average particle size of less than 1 .mu.m.

7. The composition of claim 1 comprising apatite having an average particle size of less than 0.5 .mu.m.

8. The composition of claim 1 comprising apatite having an average particle size of less than 0.25 .mu.m.

9. A composition comprising particulate apatite having a surface area of at least 40 m.sup.2 /g and a spherical crystal.

10. The composition of claim 7 comprising particulate apatite having a surface area of at least 100 m.sup.2 /g.

11. The composition of claim 9 comprising particulate apatite having a surface area of at least 150 m.sup.2 /g.

12. The composition of claim 9 that undergoes apatite phase decomposition of less than 10% when exposed to conditions of at least 1000.degree. C. for at least 2 hours.

13. The composition of claim 12 that undergoes apatite phase decomposition of less than 5% when exposed to conditions of at least 1000.degree. C. for at least 2 hours.

14. The composition of claim 12 that undergoes apatite phase decomposition of less than 3% when exposed to conditions of at least 1000.degree. C. for at least 2 hours.

15. The composition of claim 12 that undergoes apatite phase decomposition of less than 10% when exposed to conditions of at least 1100.degree. C. for at least 2 hours.

16. The composition of claim 12 that undergoes apatite phase decomposition of less than 5% when exposed to conditions of at least 1100.degree. C. for at least 2 hours.

17. The composition of claim 12 that undergoes apatite phase decomposition of less than 3% when exposed to conditions of at least 1100.degree. C. for at least 2 hours.

18. The composition of claim 12 that undergoes apatite phase decomposition of less than 10% when exposed to conditions of at least 1200.degree. C. for at least 2 hours.

19. The composition of claim 12 that undergoes apatite phase decomposition of less than 5% when exposed to conditions of at least 1200.degree. C. for at least 2 hours.

20. The composition of claim 12 that undergoes apatite phase decomposition of less than 3% when exposed to conditions of at least 1200.degree. C. for at least 2 hours.

21. The composition of claim 12 that undergoes apatite phase decomposition of less than 10% when exposed to conditions of at least 1300.degree. C. for at least 2 hours.

22. The composition of claim 12 that undergoes apatite phase decomposition of less than 5% when exposed to conditions of at least 1300.degree. C. for at least 2 hours.

23. The composition of claim 12 that undergoes apatite phase decomposition of less than 3% when exposed to conditions of at least 1300.degree. C. for at least 2 hours.

25. The article of claim 24 wherein the particulate apatite is consolidated.

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L13: Entry 34 of 37

File: USPT

US-PAT-NO: 5510118
DOCUMENT-IDENTIFIER: US 5510118 A

TITLE: Process for preparing therapeutic compositions containing nanoparticles

DATE-ISSUED: April 23, 1996

INVENTOR-INFORMATION:

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Mueller; Ronald L.	Downingtown	PA		
Swanson; Jon R.	Macungie	PA		
Mishra; Dinesh S.	Harleysville	PA		

US-CL-CURRENT: 424/489; 424/488, 424/490

CLAIMS:

What is claimed is:

1. A process for preparing particles consisting essentially of 99.9-10% by weight of a crystalline drug substance having a solubility in water of less than 10 mg/ml, said drug substance having a non-crosslinked surface modifier adsorbed on the surface thereof in an amount of (). 1-9()% by weight and sufficient to maintain an effective average particle size of less than about 40 nm, said process comprises the steps of:

a) preparing a promix of said crystalline drug substance having a particle size of less than about 100 .mu.m and said surface modifier by mixing them in a liquid dispersion medium being selected form the group consisting of water, aqueous salt solutions, safflower oil, ethanol, t-butanol, hexane and glycol;

b) transferring said premix to a microfluidizer having an interaction chamber capable of producing shear, impact, cavitatio and attrition forces;

c) subjecting said promix to said forces at a temperature not exceeding 40.degree. C. and a fluid pressure of from about 3,000 to about 30,000 psi by passing said premix through said

interaction chamber to reduce the particle size of said drug substance and to obtain a homogeneous slurry thereof:

d) collecting all the slurry from said interaction chamber into a receiving tank;

c) reintroducing said slurry m said receiving tank into said interaction chamber to further subject said slurry to said forces and thereby to decrease the effective average particle size of said drub substance: and

f) repeating said collection and reintroduction steps until said drug substance is reduced to an effective average particle size o less than about 400 nm.

2. The process of claim 1 wherein said particles have an effectiv particle size of less than 250 nm.

3. The process of claim 1 wherein said particles have an effectiv particle size of less than 100 .mu.m.

4. The process of claim 1 wherein said drug substance is selected from the group consisting of: analgesics, anti-inflammatory agents, anthelmintics, anti-arrhythmic agents, antibiotics, anticoagulants, antidepressants, antidiabetic agents, antiepileptics, antihistamines, antihypertensive agents, antimuscarinic agents, antimycobacterial agents, antineoplastic agents, immunosuppressants, antithyroid agents, antiviral agents, anxiolytic sedatives, astringents, beta-adrenoceptor blocking agents, contrast media, corticosteroids, cough suppressants, diuretics, dopaminergics, haemostatics, immufiological agents, lipid regulating agents, muscle relaxants, parasympathomimetics, parathyroid calcitonin, prostaglandins, radio-pharmaceuticals, se hormones, anti-allergic agents, stimulants, sympathomimetics, thyroid agents, vasoclilators and xanthines.

5. The process of claim 1 wherein said drug substance is a steroid.

6. The process of claim 1 wherein said said drug substance is selected from the group consisting of: (Danazol), 5.alpha.,17.alpha.,- 1'-(methylsulfonyl)-1'H-pregn-20-yno-pyrazol17-ol, piposulfam, piposulfan, camptothecin and ethyl-3,5-diacetoamido-2,4-6triiodobenzoate.

7. The process of claim 1 wherein said surface modifier is

selected from the group consisting of: gelatin, casein, lecithin, gum acacia, cholesterol, tragacanth, stearic acid, benzalkonium chloride, calcium stearate, glyceryl monostearate, cetostearyl alcohol, cetomacrogol emulsifying wax, sorbitan esters, polyoxyethylene alkyl ethers, polyoxyethylene caster oil derivatives, polyoxyethylene sorbitan fatty acid esters, polyethylene glycols, polyoxyethylene stearates, colloidol silico dioxide, phosphates, sodium dodecylsulfate, carboxymethylcellulos calcium, carboxymethylcellulose sodium, methylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, hydroxypropylmethycellulose phthalate, noncrystalline cellulose, magnesium aluminum silicate, triethanolamine, polyvinyl alcohol, and polyvinylpyrrolidone.

8. The process of claim 1 wherein said surface modifier is selected from the group consisting of: an ethylene oxide-propylen oxide block co-polymer, lecithin, an alkyl aryl polyether sulfonate, gum acacia, sodium dodecylsulfate, and a dioctylester of sodium sulfosuccinic acid.

9. A pharmaceutical composition comprising the particles prepared by the process of claim 1 in Combination with a pharmaceutically acceptable carrier.

10. A method of treating a mammal comprising the step of administering to the mammal an effective amount of the pharmaceutical composition of claim 9.

11. A process for preparing particles consisting essentially of 99.9-10% by weight of a crystalline drug substance having a solubility in water of less than 10 mg/ml, said drug substance having a non-crosslinked surface modifier adsorbed on the surface thereof in an amount of 0.1-90% by weight and sufficient to maintain an effective average particle size of less than about 40 nm, said process comprises the steps of:

a) preparing a promix of said crystalline drug substance having a particle size of less than about 100 .mu.m and said surface modifier by mixing them in a liquid dispersion medium being selected form the group consisting of water, aqueous salt solutions, safflower oil, ethanol, t-butanol, hexane and glycol;

b) transferring said premix to a microfluidizer having an interaction chamber capable producing shear, impact, cavitation and attrition forces;

c) subjecting said premix to said forces at a temperature not exceeding 40.degree. C. and a fluid pressure of from about 3,000 to about 30,000 psi by passing said premix through said interaction chamber to reduce the particle size of said drug substance and to obtain a homogeneous slurry thereof;

d) collecting a portion of the slurry from said interaction chamber into a receiving tank:

c) reintroducing said portion of the slurry into said interaction chamber; repeating said collection and reintroduction steps in a continuous process until said drug substance is reduced to an effective average particle size of less than about 400 nm.

12. The process of claim 11 wherein said particles have an effective particle size of less than 250 nm.

13. The process of claim 11 wherein said particles have an effective particle size of less than 100 .mu.m.

14. The process of claim 11 wherein said drug substance is selected from the group consisting of: analgesics, anti-inflammatory agents, anthelmintics, anti-arrhythmic agents, antibiotics, antic oagul ants, antidepressants, antidiabetic agents, antiepileptics, antihistamines, antihypertensive agents, antimuscarinic agents, antimycobacterial agents, antineoplastic agents, immunosuppressants, antithyroid agents, antiviral agents, anxiolytic sedatives, astringents, beta-adrenoceptor blocking agents, contrast media, corticosteroids, cough suppressants, diuretics, dopaminergics, haemostatics, immuriological agents, lipid regulating agents, muscle relaxants, parasympathomimetics, parathyroid calcitonin, prostaglandins, radio-pharmaceuticals, se hormones, anti-allergic agents, stimulants, sympathomimetics, thyroid agents, vasodilators and xanthines.

15. The process of claim 11 wherein said drug substance is a steroid.

16. The process of claim 11 wherein said drug substance is selected from the group consisting of: (Danazol), 5.alpha., 17.alpha.,- 1'-(methylsulfonyl)- 1'H-pregn-20-yno-pyrazol-17-ol, piposulfam, piposulfan, camptothecin and ethyl-3,5-diacetoamido-2,4-6-triiodobenzoate.

17. The process of claim 11 wherein said surface modifier is selected from the group consisting of: gelatin, casein, locithin,

gum acacia, cholesterol, tragaeanth, stearic acid, benzalkonium chloride, calcium stearate, glyccryl monostearate, cetostearyl alcohol, cetomacrogol emulsifying wax, sorbitan esters, polyoxyethylcne alkyl ethers, polyoxyethylene caster oil derivatives, polyoxyethylene sorbitan htty acid esters, polyethylene glycols, polyoxyethylcne stearates, colloidel silico dioxide, phosphates, sodium dodecylsulfate, carboxymethylcellulos calcium, carboxymethylcellulose sodium, methylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, hydroxypropylmethycellulose phthalate, noncrystalline cellulose, magnesium aluminum silicate, triethanolamine, polyvinyl alcohol, and polyvinylpyrrolidone.

18. The process of claim 11 wherein said surface modifier is selected from the group consisting of: an ethylene oxide-propylen oxide block co-polymer, lecithin, an alkyl aryl polyether sulfonate, gum acacia, sodium dodecylsulfate, and a dioctylester of sodium sulfosuccinic acid.

19. A pharmaceutical composition comprising the particles prepare by the process of claim 11 in combination with a pharmaceutically acceptable carrier.

20. A method of treating a mammal comprising the step of administering to the mammal an effective amount of the pharmaceutical composition of claim 19.

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L13: Entry 34 of 37 File: USPT

DOCUMENT-IDENTIFIER: US 5510118 A
TITLE: Process for preparing therapeutic compositions containing nanoparticles

Brief Summary Text (3):
This invention relates to a process for preparing therapeutic compositions containing nanoparticles.

Brief Summary Text (11):
U.S. Pat. No. 5,145,684 discloses a process for preparing particles consisting of a crystalline drug substance having a surface modifier or surface active agent adsorbed on the surface of the particles in an amount sufficient to maintain an average particle size of less than about 40 nanometers. The process of preparation comprises the steps of dispersing the drug substance in a liquid dispersion medium and applying mechanical means in the presence of grinding media to reduce the particle size of the drug substance to an average particle size of less than 4 nm. The particles can be reduced in the presence of a surface active agent or, alternatively, the particles can be contacted with a surface activ agent after attrition. The presence of the surface active agent prevents flocculation/agglomeration of the nanoparticles.

Brief Summary Text (17):
1) U.S. Pat. No. 5,342,609, directed to methods of preparing solid apatite particles used in magnetic resonance imaging, x-ray and ultrasoun

Brief Summary Text (26):
10) R. Bodmeier, H. Chen, P. Tyle, and P. Jarosz, "Spontaneous Formation of Drug-Containing Acrylic Nanoparticles," J. Microencap, 8, 161-170 (1991).

Brief Summary Text (32):
In accordance with the present invention, there is provided a process of preparing stable, dispersible, water-insoluble, drug nanoparticles consisting essentially of a crystalline drug substance having a surface modifier adsorbed on the surface thereof comprising the steps of:

Brief Summary Text (38):
It is an advantageous feature that a wide variety of surface modified drug nanoparticles free of unacceptable contamination can be prepared i accordance with this invention.

Detailed Description Text (2):
This invention is based partly on the discovery that drug particles having an extremely small effective avenge particle size can be prepared b milling in a microfluidizer in conjunction with a surface modifier, and that such particles are stable and do not appreciably flocculate or agglomerate due to interparticle attractive forces and can be formulated into pharmaceutical compositions exhibiting unexpectedly high bioavailability. While the invention is described herein primarily in connection with its preferred utility, i.e., with respect to nanoparticulate drug substances for use in pharmaceutical compositions, it is also believed to be useful in other applications such as the formulation of particulate cosmetic compositions and the preparation of particulate dispersions for use in image and magnetic recording elements.

Detailed Description Text (41):
The resulting dispersion of this invention is stable and consists of the liquid dispersion medium and the above-described particles. The dispersion of surface modified drug nanoparticles can be spray coated onto sugar spheres or onto a pharmaceutical excipient in a fluid-bed spray coater by techniques well known in the art.

Other Reference Publication (8):
R. Bodmeier, H. Chen, P. Tyle, and P. Jarosz, "Spontaneous Formation of Drug-Containing Acrylic Nanoparticles," J. Microencap, 8, 161-1 (1991).

CLAIMS:

1. A process for preparing particles consisting essentially of 99.9-10% by weight of a crystalline drug substance having a solubility in water

less than 10 mg/ml, said drug substance having a non-crosslinked surface modifier adsorbed on the surface thereof in an amount of (). 1-9()% by weight and sufficient to maintain an effective average particle size of less than about 400 nm, said process comprises the steps of:

f) repeating said collection and reintroduction steps until said drug substance is reduced to an effective average particle size of less than abou 400 nm.

2. The process of claim 1 wherein said particles have an effective particle size of less than 250 nm.

11. A process for preparing particles consisting essentially of 99.9-10% by weight of a crystalline drug substance having a solubility in wate less than 10 mg/ml, said drug substance having a non-crosslinked surface modifier adsorbed on the surface thereof in an amount of 0.1-90% weight and sufficient to maintain an effective average particle size of less than about 400 nm, said process comprises the steps of:

c) reintroducing said portion of the slurry into said interaction chamber; repeating said collection and reintroduction steps in a continuous process until said drug substance is reduced to an effective average particle size of less than about 400 nm.

12. The process of claim 11 wherein said particles have an effective particle size of less than 250 nm.

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L13: Entry 34 of 37 File: USPT Apr 23, 1996

US-PAT-NO: 5510118
DOCUMENT-IDENTIFIER: US 5510118 A

TITLE: Process for preparing therapeutic compositions containing nanoparticles

DATE-ISSUED: April 23, 1996

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Swanson; Jon R.	Macungie	PA		
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APPL-NO: 08/ 388092 [PALM]
DATE FILED: February 14, 1995

INT-CL: [06] A61 K 9/14

US-CL-ISSUED: 424/489; 424/488, 424/490
US-CL-CURRENT: 424/489; 424/488, 424/490

FIELD-OF-SEARCH: 424/488, 424/489, 424/490, 424/22

PRIOR-ART-DISCLOSED:

U.S. PATENT DOCUMENTS

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PAT-NO	ISSUE-DATE	PATENTEE-NAME	US-CL
4107288	August 1978	Oppenheim et al.	424/22
4540602	September 1985	Motoyama et al.	427/213.31
5039527	August 1991	Tabibi et al.	424/450
5118528	June 1992	Fessi et al.	427/213.36
5145684	September 1992	Liversidge et al.	424/489
5228905	July 1993	Grunewalder et al.	106/2
5342609	August 1994	Meeh et al.	424/9
5399363	March 1995	Liversidge et al.	424/490

OTHER PUBLICATIONS

Lachman et al, The Theory and Practice of Industrial Pharmacy, Chapter 2, "Milling", p. 45, (1986).
G. Gregoriadis, H. Da Silva, and A. T. Florence, "A Procedure for the Efficient Entrapment of Drugs in Dehydration-Rehydration Liposome (DRVs)", Int. J. Pharm. 65, 235-242 (1990).
E. Doegito, H. Fessi, M. Appel, F. Puisieux, J. Bolard, and J. P. Devissaguet, "New Techniques for Preparing Submicronic Emulsions--Application to Amphotericine-B" STP Pharma Sciences 4, 155-162 (1994).
D. M. Lidgate, R. C. Fu, N. E. Byars, L. C. Foster, and J. S. Fleitman, "Formulation of Vaccine Adjuvant Muramyldipeptides. Part 3. Processing Optimization, Characterization and Bioactivity of an Emulsion Vehicle," Pharm Res. 6, 748-752 (1989).
H. Talsma, A. Y. Ozer, L. VanBloois, and D. J. Crommelin, "The Size Reduction of Liposomes with a High Pressure Homogenizer (Microfluidizer): Characterization of Prepared Dispersions and comparison with Conventional Methods," Drug Dev. Ind. Pharm. 15, 197-20 (1989).
D. M. Lidgate, T. Trattner, R. M. Shultz, and B. Maskiewicz, "Sterile Filtration of a Parenteral Emulsion," Pharm. Res. 9, 860-863 (1990).
R. Bomeier, and H. Chen, "Indomethacin Polymeric Nanosuspensions Prepared by Microfluidization," J. Contr. Rel. 12, 223-233 (1990).
R. Bodmeier, H. Chen, P. Tyle, and P. Jarosz, "Spontaneous Formation of Drug-Containing Acrylic Nanoparticles," J. Microencap, 8, 161-1 (1991).
F. Koosha, and R. H. Muller, "Nanoparticle Production by Microfluidization," Archiv Der Pharmazie 321, 680 (1988).
The Extra Pharmapoeia, by Martindale, 29th Edition, The Pharmaceutical Press, London, 1989.

ART-UNIT: 152

PRIMARY-EXAMINER: Page; Thurman K.

ASSISTANT-EXAMINER: Benston, Jr.; William E.

ABSTRACT:

A process of preparing nanoparticulate drug substances comprising the steps of: preparing a premix of the drug substance and a surface modifier, and subjecting the premix to mechanical means to reduce the particle size of the drug substance, the mechanical means producing shear, impact, cavitation and attrition.

20 Claims, 0 Drawing figures

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(3 AND (DENTIFRICE OR TOOTHPASTE)).USPT,JPAB,EPAB,DWPI,TDBD.	0
(L3 AND (DENTIFRICE OR TOOTHPASTE)).USPT,JPAB,EPAB,DWPI,TDBD.	0

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L15	l3 and stomatol?	0	L15
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L10	l1 and (whiskers or rodlike or barlike or needle crystals or particle length? or nanometers or nanocrystals or nanoparticles or rod-shaped or bar-shaped or 20nm or 70 nm or 5 nm or 10 nm or 40 nm or 50 nm or 35 nm or 30 nm or 130 nm or 50 nanometers or 150 nanometers)	3756	L10
L9	l8 and diameter? and length?	12	L9
L8	l3 and (toothpaste or dentifrice or stomatol? or teeth or dental)	48	L8
L7	l5 and l2	0	L7
L6	l5 and nano?.clm.	0	L6
L5	l1 and nano?	35	L5
L4	l3 and crystals and particle size	32	L4
L3	l1 and (anisometric or anisotropic)	307	L3
L2	l1 and agglomeration	879	L2
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Term	Documents
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TOOTHPASTE.DWPI,TDBD,EPAB,JPAB,USPT.	10269
(10 AND (DENTIFRICE OR TOOTHPASTE)).USPT,JPAB,EPAB,DWPI,TDBD.	50
(L10 AND (DENTIFRICE OR TOOTHPASTE)).USPT,JPAB,EPAB,DWPI,TDBD.	50

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Search: L17

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Search History

DATE: Wednesday, July 31, 2002 Printable Copy Create Case

Set Name side by side	**Query**	**Hit Count**	**Set Na** result s
	DB=USPT,JPAB,EPAB,DWPI,TDBD; PLUR=NO; OP=ADJ		
L17	l10 and (dentifrice or toothpaste)	50	L17
L16	l3 and (dentifrice or toothpaste)	0	L16
L15	l3 and stomatol?	0	L15
L14	l13 and (surfactant? or surface active agent? or wetting agent? or protective colloid?)	22	L14
L13	l11 and agglomerat?	37	L13
L12	l11 and particle?.clm.	126	L12
L11	l10 and (nano?.clm. or nm.clm. or nanometers.clm. or nanometer?.clm.)	416	L11
L10	l1 and (whiskers or rodlike or barlike or needle crystals or particle length? or nanometers or nanocrystals or nanoparticles or rod-shaped or bar-shaped or 20nm or 70 nm or 5 nm or 10 nm or 40 nm or 50 nm or 35 nm or 30 nm or 130 nm or 50 nanometers or 150 nanometers)	3756	L10
L9	l8 and diameter? and length?	12	L9
L8	l3 and (toothpaste or dentifrice or stomatol? or teeth or dental)	48	L8
L7	l5 and l2	0	L7
L6	l5 and nano?.clm.	0	L6
L5	l1 and nano?	35	L5
L4	l3 and crystals and particle size	32	L4
L3	l1 and (anisometric or anisotropic)	307	L3
L2	l1 and agglomeration	879	L2
L1	(calcium phosphate or apatite or hydroxylapatite or hydroxyapatite or calcium fluoride or fluorapatite o0r amorphous calcium phosphate or fluorophosphate calcium or calcium fluorophosphate or fluorine-doped hydroxylapatite or f-doped hydroxylapatite)	47239	L1

END OF SEARCH HISTORY

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L17: Entry 15 of 50 File: USPT

US-PAT-NO: 6117456
DOCUMENT-IDENTIFIER: US 6117456 A

TITLE: Methods and products related to the physical conversion of reactive amorphous calcium phosphate

DATE-ISSUED: September 12, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Lee; Dosuk D.	Brookline	MA		
Rey; Christian	Castanet			FR
Aiolova; Maria	Brookline	MA		
Tofighi; Aliassghar	Belmont	MA		

US-CL-CURRENT: 424/602; 106/690, 423/308, 423/311, 424/484, 623/23.37, 623/23.48, 623/23.62

CLAIMS:

What is claimed is:

1. A reactive amorphous calcium phosphate material having at leas 90% percent amorphous character and characterized in that, when prepared 1:1 as a mixture with dicalcium diphosphate in water, th mixture remains injectable and formable for a time greater than about 60 minutes at about 25.degree. C. and hardens at about 37.degree. C. within about 10 to about 60 minutes.

2. The amorphous calcium phosphate material of claim 1, having a specific surface area of greater than about 100 sq. m/g.

3. The amorphous calcium phosphate material of claim 1, wherein the specific surface area is about 120 sq. m/g.

4. The amorphous calcium phosphate of claim 1 or 2, further characterized as having an average pore size of 130 .ANG..

5. The amorphous calcium phosphate of claim 1, wherein the mixtur hardens within about 10 to 30 minutes at about 37.degree. C.

6. The amorphous calcium phosphate of claim 1, wherein the calciu to phosphate ratio is about 1.55 to 1.65.

7. The amorphous calcium phosphate of claim 1, wherein said reactivity is obtained by introduction of chemical vacancies into the material.

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L17: Entry 15 of 50 File: USPT Sep 12, 2000

US-PAT-NO: 6117456
DOCUMENT-IDENTIFIER: US 6117456 A

TITLE: Methods and products related to the physical conversion of reactive amorphous calcium phosphate

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Lee; Dosuk D.	Brookline	MA		
Rey; Christian	Castanet			FR
Aiolova; Maria	Brookline	MA		
Tofighi; Aliassghar	Belmont	MA		

ASSIGNEE-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY	TYPE CODE
Etex Corporation	Cambridge	MA			02

APPL-NO: 08/ 729344 [PALM]
DATE FILED: October 16, 1996

PARENT-CASE:
This application is a continuation-in-part application of co-pending application U.S. Ser. No. 08/650,764 filed May 20, 1996 entitled "Nove Bone Substitution Material and a Method of Its Manufacture", which is a continuation-in-part application of application U.S. Ser. No. 08/446,182 filed M.kay 19, 1995 entitled "Synthesis of Reactive Amorphous Calcium Phosphates", now U.S. Pat. No. 5,676,976 both of wh are herein incorporated in its entirety by reference. This application also is related to several co-pending applications filed on even day herewith, entitled, "Bioresorbable Ceramic Composites" U.S. Ser. No. 08/732,016, "Delivery Vehicle" U.S. Ser. No. 08/729,342, "Cell Seed of Ceramic Compositions" U.S. Ser. No. 08/729,354 and "Orthopedic and Dental Ceramic Implants" U.S. Ser. No. 08/729,343, each of whic is incorporated by reference.

INT-CL: [07] A61 K 47/02

US-CL-ISSUED: 424/602; 424/484, 623/16, 423/308, 423/311, 106/690
US-CL-CURRENT: 424/602; 106/690, 423/308, 423/311, 424/484, 623/23.37, 623/23.48, 623/23.62

FIELD-OF-SEARCH: 523/115, 523/218, 523/219, 523/116, 428/404, 428/403, 264/4, 264/4.7, 264/4.3, 264/4.46, 106/690, 106/691, 106/6 623/16, 424/484, 424/602, 423/308, 423/311

PRIOR-ART-DISCLOSED:

U.S. PATENT DOCUMENTS

Search Selected | Search ALL

	PAT-NO	ISSUE-DATE	PATENTEE-NAME	US-CL
☐	Re33161	February 1990	Brown et al.	
☐	Re33221	May 1990	Brown et al.	

☐	4157378	June 1979	Tomlinson et al.	
☐	4429691	February 1984	Niwa et al.	
☐	4612053	September 1986	Brown et al.	
☐	4684673	August 1987	Adachi	523/116
☐	4737411	April 1988	Graves, Jr. et al.	
☐	4849193	July 1989	Palmer et al.	
☐	4880610	November 1989	Constantz	
☐	4917702	April 1990	Scheicher et al.	
☐	4938938	July 1990	Ewers et al.	
☐	4959104	September 1990	Iino et al.	
☐	5034059	July 1991	Constantz	
☐	5037639	August 1991	Tung	
☐	5047031	September 1991	Constantz	
☐	5053212	October 1991	Constantz et al.	
☐	5085861	February 1992	Gerhart et al.	
☐	5129905	July 1992	Constantz	
☐	5149368	September 1992	Liu et al.	
☐	5152836	October 1991	Hirano et al.	
☐	5164187	November 1992	Constantz et al.	
☐	5178845	January 1993	Constantz et al.	
☐	5262166	November 1993	Liu et al.	
☐	5279831	January 1994	Constantz et al.	
☐	5281265	January 1994	Liu	
☐	5286763	February 1994	Gerhart et al.	
☐	5336264	August 1994	Constantz et al.	
☐	5342441	August 1994	Mandai et al.	
☐	5352715	October 1994	Wallace et al.	
☐	5427754	June 1995	Nagata et al.	
☐	5470803	November 1995	Bonfield et al.	
☐	5496399	March 1996	Ison et al.	
☐	5501706	March 1996	Arenberg	623/16
☐	5516532	May 1996	Atala et al.	
☐	5522893	June 1996	Chow et al.	
☐	5525148	June 1996	Chow et al.	
☐	5542973	August 1996	Chow et al.	
☐	5545254	August 1996	Chow et al.	
☐	5562895	October 1996	Tung	424/57
☐	5565502	October 1996	Glimcher et al.	523/115
☐	5605713	February 1997	Boltong	427/2.1
☐	5626861	May 1997	Laurencin et al.	424/426
☐	5665120	September 1997	Ohtsuka et al.	
☐	5683461	November 1997	Lee et al.	623/16
☐	5691397	November 1997	Glimcher et al.	523/115
☐	5770289	June 1998	Breitbart et al.	

☐	5782971	July 1998	Constantz et al.	
☐	5846312	December 1998	Ison et al.	106/690

FOREIGN PATENT DOCUMENTS

FOREIGN-PAT-NO	PUBN-DATE	COUNTRY	US-CL
0 268 463	May 1988	EP	
0347028	April 1989	EP	
0664133	February 1994	EP	
63-111875	May 1988	JP	
63-170205	July 1988	JP	
2-182261	July 1990	JP	
5-305134	November 1993	JP	
06228011	December 1994	JP	
7277712	October 1995	JP	
92/001009	January 1992	WO	
92/02453	February 1992	WO	
94/04657	August 1993	WO	
94/20064	September 1994	WO	
95/08319	September 1994	WO	
94/02412	July 1995	WO	
96/36562	May 1996	WO	
97/17285	November 1996	WO	

OTHER PUBLICATIONS

Rey et al,. "Chemical Properties of Poorly Crystalline Apatites" Phosphorus Res. Bull. 6:67-70 (1996) abstract only.
Abboudi et al., "Development of organic and polymer carriers for demineralized bone matrix: Effect on bone cell behavior," Fifth World Congress, May 29-Jun.2, 1996, Toronto, Canada.
Athanasou et al., "Current Concepts Review: Cellular Biology of Bone-Resorbing Cells", J. Bone and Joint Surg., 78-A: 1096-1112, 1996.
Appel et al., "Recent advances in implants for bone growth promotion", Exp. Opin. Ther. Patents 4:1461, 1994.
Attawia et al. "The long term osteoblast response to poly (anhydride-co-imides): A new degradable polymer for use in bone," Fifth World Congress, May 29-Jun. 2, 1996, Toronto Canada.
Blumenthal et al., "Effect of Preparation Conditions on the Properties and Transformation of Amorphous Calcium Phosphate", Mat Res. Bu 7(11):1181 (Nov. 1972).
Boskey, Adele L., "Matrix Proteins and Mineralization: An Overview", Connect. Tiss. Res., 35 (1-4): 357-363, 1996.
Denissen et al., "Net-shaped hydroxyapatite implants for release of agents modulating periodontal-like tissues", J. Periodontal Res., 32:40-46 1997.
Driessens et al., "Calcium Phosphate Bone Cements", Encyc. Hand. Biomat. and Bioeng., 855-877, 1995.
Fukase "Stetting Reactions and Compressive Strengths of Calcium Phosphate Cements", J. Dent. Res 69(12):1852 (Dec. 1990).
Gao, T.J., "Established compentence of bioactive composite bone substitute on the healing of diaphseal segmental defects in sheep," Fifth World Congress, May 29-Jun. 2, 1996, Toronto, Canada.
Graves et al., "Resorbable ceramic implants", J.Biomed. Mater. Res., No. 324, p.55, 1996.
Hollinger et al., "Role of Substitutes" Clin. Ortho & Related Res., No. 324, p. 55, 1996.
Hubbell, "Biomaterials in tissue engineering", Bio/Technology, 13;56, 1995.
Kim et al., "Hyaluronan-based biodegradable scaffolds for skeletal tissue reconstruction," Fifth World Biomaterials Congress, May 29-Jun. 1996, Toronto, Canada.
Kinoshita et al., Reconstruction of mandibular discontinuity defects in dogs using autogenic particulate cancellous bone and marrow and poly(L-lactide) mesh, Fifth World Biomaterials Congress, May 29-Jun. 2, 1996, Toronto, Canada.
Oka et al., "Development of artificial osteochondral composite material", Fifth World Biomaterials Congress, May 29-Jun. 2, 1996, Toronto Canada.
Rizkalla et al., "Effect of composition on strength of bioactive composites," Fifth World Biomaterials Congress, May 29-Jun. 2, 1996, Toron Canada.
Selmani et al., "Bioerodible polyster foams for orthopaedic tissue culture", Fifth World Biomaterials Congress, May 29-Jun. 2, 1996, Toron Canada.
Shindo et al., "Facial Skeletal Augmentation Using Hydroxyapatite Cement", Arch Otolaryngol Head Neck Surg -vol. 119, Feb. 1993.

Thissen et al., "Surface modification of bioresorbable polymers by plasma induced graft polymerization", Fifth World Biomaterials Congres May 29-Jun. 2, 1996, Toronto.
Tormala, "Biodegradable self-reinforced composite materials; manufacturing structure and mechanical propertiesd", Clin. Mat., 10:29, 1992
Yasue et al. "Effect of Adsorption of Succinic Acid on the Formation of Amorphous Calcium Phosphate" J. Ceram. Soc. Japan 102 (12):1 (D 1994).
Hayes et al. "Augmentation of Cementless Femoral Stems to Improve Initial Stability Using a Remodelable Calcium-Phosphate Bone Miner Substitute" 61st Annual American Academy of Orthodaedic Surgeons Meeting, New Orleans, Feb. 1994.
Aoki, "Science and medical applications of hydroxyapatite", JAAS, pp. 11-15, 1991.
Barton et al., "Surface and bulk properties of amorphous calcium phosphate" Colloid Interface Sci. [Proc. Int. Conf.], 50th 3:71 (1976) [CA 87:73954v] (Abstract).
Besic et al., "Electron probe microanalysis of noncarious enamel and dentin and calcified tissues in mottled teeth", J. Dent. Res., 48:131 (19

Constantz et al., "Skeletal repair by in situ formation of the mineral phase of bone", Science, 267: 1976 (1995).
Eanes et al., "Intermediate states in the precipitation of hydroxyapatite", Nature, 208: 365-367 (1965).
Eanes et al., "Intermediate phases in the basic solution preparation of alkaline earth phosphates" Calcified Tissue Res., 2(1):38 (1968) [CA 69:110373f] (Abstract).
Eanes, "Thermochemical studies on amorphous calcium phsophate", Calc. Tiss. Res., 5:133 (1970).
Glimcher et al., "Recent studies of the mineral phase in bone and its possible linkage to the organic matrix by protein-bound phosphate bond Phil. Trans. R. Soc. Lond. B 304:479-508 (1984).
Greenfield et al., "Formation chemistry of amorphous calcium phosphates prepared from carbonate containing solutions", Calc. Tiss. Res., 9:152 (1972).
Hirasawa et al., "Manufacture of high purity hydroxyapatite," Chemical Abstracts, 108 (10), p. 166, No. 78193h (Mar. 7, 1988).
Holmes et al., "Surface areas by gas adsorption on amorphous calcium phosphate and crystalline hydroxyapatite", Calc. Tiss. Res., 7:163 (1971).
Ishikawa et al., "Effects of preparation in aqueous solution on properties of hydroxyapatites", Dent. Mater. J. 9(1):58 (1990) [CA 113:21816 (Abstract).
Labarthe et al., "Sur la structure et les properietes des apatites carbonatees de type B phospho-calciques", Ann. Chem., 8:289 (1973).
Nylen et al., "Molecular and ultrastructural studies of non-crystalline calcium phosphates", Calc. Tiss. Res., 9:95 (1972).
Otsuka et al., "Effect of particle size of metastable calcium phosphates on mechanical strength of a novel self-setting bioactive calcium phosphate", J. Biomed Mat. Res., 29:25 (1995).
Pool, "Coral chemistry leads to human bone repair", Science, 269;1772 (Mar. 1995).
Posner et al., "Synthetic amorphous calcium phsophate and its relation to bone mineral structure", Bone Mineral Structure, 8:273-281 (1975
Rey et al., "The carbonate environment in bone mineral: a resolution-enhanced fourier transform infared spectroscopy study", Calcif. Tissue Int., 45:157 (1989).
Rey et al., "Structural studies of the mineral phase of calcifying cartilage", J. Bone Min. Res., 6:515 (1991).
Rey et al., "Preparation of Microporous Ceramic at Low Temperature from Poorly Crystalline Apatite", Symposium Abstract, 1993.
Termine et al., "Amorphous/Crystalline Interrelationships in Bone Mineral", Calc. Tiss. Res. 1, 8-23 (1967).
Tung et al., "An intermediate state in hydrolysis of amorphous calcium phosphate", Calcif. Tissue Int., 35:783 (1983).

ART-UNIT: 167

PRIMARY-EXAMINER: Levy; Neil S.

ABSTRACT:

The present invention provides a novel process for producing a calcium phosphate cement or filler which hardens in a temperature dependen fashion in association with an endothermic reaction. In the reaction a limited amount of water is mixed with dry calcium phosphate precurso produce a hydrated precursor paste. Hardening of the paste occurs rapidly at body temperature an is accompanied by the conversion of one o more of the reactants to poorly crystalline apatitic calcium phosphate. The hardened cements, fillers, growth matrices, orthopedic and delive devices of the invention are rapidly resorbable and stimulate hard tissue growth and healing.

7 Claims, 27 Drawing figures

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L17: Entry 30 of 50 File: USPT

US-PAT-NO: 5783217
DOCUMENT-IDENTIFIER: US 5783217 A

TITLE: Low temperature calcium phosphate apatite and a method of its manufacture

DATE-ISSUED: July 21, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Lee; Dosuk D.	Brookline	MA		
Rey; Christian	Castanet			FR
Aiolova; Maria	Brookline	MA		
Tofighi; Ali	Belmont	MA		

US-CL-CURRENT: 424/602; 264/234, 423/308, 423/311, 428/704, 514/2

CLAIMS:

What is claimed is:

1. A method of preparing a low crystallinity calcium phosphate apatite, comprising:

precipitating a low crystallinity calcium phosphate from an aqueous solution comprising calcium and phosphate ions;

collecting the low crystallinity calcium phosphate from the solution; and

dehydrating the low crystallinity calcium phosphate in a relative humidity of less than 100% and at a temperature to obtain a low crystallinity calcium phosphate apatite block solid.

2. The method of claim 1, further comprising:

casting the low crystallinity calcium phosphate into a mold befor dehydration.

3. The method of claim 1, wherein the aqueous solution is selecte to provide a calcium to phosphate ratio in the range of about 1.3 to 1.7.

4. The method of claim 1, wherein the aqueous solution is selecte to provide a calcium to phosphate ratio in the range of about 1.5 to 1.68.

5. The method of claim 1, wherein the precipitation is carried ou in the aqueous solution further comprising carbonate ions.

6. The method of claim 1, wherein the aqueous solution is at a pH in the range of about 6.0 to about 8.5.

7. The method of claim 1, wherein the aqueous solution is at a pH in the range of about 7.3 to about 7.5.

8. The method of claim 1, wherein the calcium and phosphate ions are introduced into the aqueous solution by fast.sub.-- addition.

9. The method of claim 1, wherein the calcium and phosphates ions are introduced into the aqueous solution by titration.

10. The method of claim 1, wherein the step of collection is selected from the group consisting of filtration, centrifugation and sedimentation.

11. The method of claim 1, wherein the aqueous solution further comprises a crystallization inhibitor.

12. The method of claim 11 wherein the inhibitor is present in a range of about 0.5 wt % to about 30 % wt total dry weight of calcium and phosphate ion sources.

13. The method of claim 11, wherein the inhibitor is selected fro the group consisting of carbonate ion, magnesium ion, and pyrophosphate ion.

14. The method of claim 1 or 11, further comprising:

maturing the low crystallinity calcium phosphate in the aqueous solution prior to collection.

15. The method of claim 14, wherein maturation is carried out for a time sufficient to obtain a calcium phosphate gel having a composition substantially similar to child's bone.

16. The method of claim 14, wherein maturation is carried out for a time sufficient to obtain a calcium phosphate gel having a composition substantially similar to adult's bone.

17. The method of claim 14, wherein maturation is carried out for a time sufficient to obtain a calcium phosphate gel having a composition substantially similar to elderly bone.

18. The method of claim 14, wherein the calcium phosphate apatite is matured for a time in the range of about one hour to about one year.

19. The method of claim 14, wherein the calcium phosphate apatite is matured for a time in the range of about two weeks to about si months.

20. The method of claim 1 or 11, wherein the step of dehydration is carried out at a temperature in the range of about 1.degree. C to about 50.degree. C.

21. The method of claim 14, wherein the step of dehydration is carried out at a temperature in the range of about 1.degree. C. t about 50.degree. C.

22. The method of claim 1, wherein the step of dehydration is carried out at a temperature in the range of about 4.degree. C. t about 37.degree. C.

23. The method of claim 1 or 11, wherein the step of dehydrating the low crystallinity calcium phosphate comprises dehydrating in humidity controlled to within the range of about 55% to about 99% RH at a temperature of less than 50.degree. C.

24. The method of claim 14, wherein the step of dehydrating the low crystallinity calcium phosphate comprises dehydrating in a humidity controlled to within the range of about 55% to about 99% RH at a temperature of less than 50.degree. C.

25. The method of claim 1 or 11, wherein the step of dehydrating the low crystallinity calcium phosphate comprises dehydrating in humidity controlled to within the range of about 60% to about 70% RH at 25.degree. C.

26. The method of claim 1 or 11, wherein step of dehydration is carried out for a time in the range of about one week to about on year.

27. The method of claim 14, wherein step of dehydration is carrie out for a time in the range of about one week to about one year.

28. The method of claim 1 or 11, wherein step of dehydration is carried out for a time in the range of about two weeks to about six months.

29. The method of claim 1 or 11, wherein step of dehydration is carried out for a time in the range of about three weeks to about four weeks.

30. The method of claim 1, further comprising the step of including a bioactive molecule into the calcium phosphate apatite

31. The method of claim 30, wherein the bioactive molecule is added to the collected precipitate before dehydration.

32. The method of claim 30, wherein the bioactive molecule is added to the aqueous solution.

33. The method of claim 30, wherein the bioactive molecule is selected from the group consisting of bone regenerative proteins, and antibiotics and its agents.

34. A method of preparing a low crystallinity calcium phosphate apatite, comprising

precipitating a low crystalline calcium phosphate from an aqueous solution comprising calcium and phosphate ions;

collecting the low crystallinity calcium phosphate from the solution; and

lyophilizing the collected precipitate to obtain a low crystallinity calcium phosphate apatite.

35. A low crystallinity calcium phosphate apatite block solid prepared according to the method of claim 1, 11 or 30.

36. A low crystallinity calcium phosphate apatite block solid prepared according to the method of claim 14.

37. The low crystallinity calcium phosphate apatite block solid o claim 35, further characterized by having a porosity in the range of about 30 .ANG. to about 100 .ANG..

38. The low crystallinity calcium phosphate apatite block solid o claim 35, further characterized by having a hardness in the range

of about 20 VHN to about 40 VHN.

39. The low crystallinity calcium phosphate apatite block solid o claim 36, further characterized by having a porosity in the range of about 30 .ANG. to about 100 .ANG..

40. The low crystallinity calcium phosphate apatite block solid o claim 36, further characterized by having a hardness in the range of about 20 VHN to about 40 VHN.

41. A low crystallinity calcium phosphate apatite characterized a a solid block material having a porosity in the range of about 30 .ANG. to about 100 .ANG. and a hardness in the range of about 20 VHN to about 40 VHN.

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L17: Entry 30 of 50 File: USPT Jul 21, 1998

US-PAT-NO: 5783217
DOCUMENT-IDENTIFIER: US 5783217 A

TITLE: Low temperature calcium phosphate apatite and a method of its manufacture

DATE-ISSUED: July 21, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Lee; Dosuk D.	Brookline	MA		
Rey; Christian	Castanet			FR
Aiolova; Maria	Brookline	MA		
Tofighi; Ali	Belmont	MA		

ASSIGNEE-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY	TYPE CODE
Etex Corporation	Cambridge	MA			02

APPL-NO: 08/ 554817 [PALM]
DATE FILED: November 7, 1995

INT-CL: [06] A61 K 33/42, C01 B 25/32

US-CL-ISSUED: 424/602; 264/234, 423/308, 423/311, 428/704, 514/2
US-CL-CURRENT: 424/602; 264/234, 423/308, 423/311, 428/704, 514/2

FIELD-OF-SEARCH: 423/308, 423/309, 423/311, 264/16, 264/19, 264/234, 424/602, 428/704, 514/2

PRIOR-ART-DISCLOSED:

U.S. PATENT DOCUMENTS

Search Selected | Search ALL

	PAT-NO	ISSUE-DATE	PATENTEE-NAME	US-CL
☐	Re33221	May 1990	Brown et al.	
☐	4612053	September 1986	Brown et al.	
☐	4849193	July 1989	Palmer et al.	
☐	4880610	November 1989	Constantz	
☐	4938938	July 1990	Ewers et al.	
☐	5037639	August 1991	Tung	
☐	5053212	October 1991	Constantz et al.	
☐	5149368	September 1992	Liu et al.	
☐	5178845	January 1993	Constantz et al.	
☐	5427754	June 1995	Nagata et al.	423/308
☐	5470803	November 1995	Bonfield et al.	
☐	5522893	June 1996	Chow et al.	623/11
☐	5525148	June 1996	Chow et al.	106/35
☐	5650176	July 1997	Lee et al.	423/308

OTHER PUBLICATIONS

Bezic et al. "Electron Probe Microanalysis of Noncarious Enamel and Dentin and Calcified Tissues in Mottled Teeth" J Dent Res. 48(1), 131-139 (Jan.-Feb., 1969).
Constantz et al. "Skeletal Repair by in Situ Formation of the Mineral Phase of Bone" Science 267, 1796-99 (Mar. 1995).
Glimcher, M.J., "Recent studies of the mineral phase in bone and its possible linkage to the organic matrix by protein-bound phosphate bond Phil. Trans. R. Soc. Londs. B 304, 479-508 (1984).
Greenfield et al., "Formation Chemistry of Amorphous Calcium Phosphates Prepared from Carbonate Containing Solutions" Calc. Tiss. Res 152-162 (1972).
Holmes et al. "Surface Areas by Gas Adsorption on Amorphous Calcium Phosphate and Crystalline Hydroxyapatite" Calc. Tiss. Res. 7, 163 (1971).
Labarthe et al. "Sur la Structure et les Proprietes des Apatites Carbonatees de Type B Phospho-Calciques" Ann. Chim. 8 (5), 289-301 (1973
Nylen et al., "Molecular and Ultrastructural Studies of Non-Crystalline Calcium Phosphates" Calc. Tiss. Res. 9, 95-108, (1972).
Pool, R. "Coral Chemistry Leads to Human Bone Repair" Science 267, 1772 (1995).
Rey et al. "The Carbonate Environment in Bone Mineral: A Resolution-Enhanced Fourier Transform Infrared Spectroscopy Study" Calcif. Tissue Int. 45, 157-164 (1989).
Rey et al. "Structural Studies of the Mineral Phase of Calcifying Cartilage" Jrnal of Bone and Mineral Research 6 (5), 515-525 (1991).
Rey et al. "Preparation of Microporous Ceramic at Low Temperature from Poorly Crystalline Apatite" Materials Research Society Symposiu V, San Francisco (1993).
Tung et al. "An Intermediate State in Hydrolysis of Amorphous Calcium Phosphate" Calcif. Tissue Int. 35, 783-790 (1983).

ART-UNIT: 113

PRIMARY-EXAMINER: Langel; Wayne

ABSTRACT:

A method of preparing a low crystallinity calcium phosphate apatite is described in which a low crystallinity calcium phosphate is precipitate from an aqueous solution comprising calcium and phosphate ions; collected from the solution; and dehydrated in a humidity and at a temperature selected to minimize growth and promote conversion to calcium phosphate apatite. The resultant calcium phosphate apatite is bl solid of improved strength, porosity and bioresorbability.

41 Claims, 3 Drawing figures

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L17: Entry 49 of 50 File: USPT

US-PAT-NO: 4587120
DOCUMENT-IDENTIFIER: US 4587120 A

TITLE: Oral composition and abrasive therefor

DATE-ISSUED: May 6, 1986

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
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Uotani; Osamu	Chiba			JP
Hayashi; Rieko	Odawara			JP

US-CL-CURRENT: 424/57; 424/49

CLAIMS:

What is claimed is:

1. A dentifrice composition comprising an abrasive consisting of calcium hydrogenphosphate anhydride whose crystallite has an average size of 300 to 3,500 angstroms as measured by X-ray diffractometry.

2. A dentifrice composition according to claim 1 wherein the calcium hydrogenphosphate anhydride has a density of 2.650 to 2.885 g/cm.sup.3, a specific surface area of 2.5 to 20 m.sup.2 /g as measured by the BET method, and an average agglomerate diamete of 2 to 30 microns.

3. A dentifrice composition according to claim 1 wherein the calcium hydrogenphosphate anhydride is in the form of a cohesive aggregate of plate crystals whose primary particle has an average size of 0.1 to 5 microns.

4. A dentifrice composition according to claim 1 wherein the calcium hydrogenphosphate anhydride is spherulitic.

5. A dentifrice composition according to claim 4 wherein the spherulitic calcium hydrogenphosphate anhydride has an average roundness of 0.45 to 0.9.

6. A dentifrice composition according to claim 2 wherein the calcium hydrogenphosphate anhydride is in the form of a cohesive aggregate of plate crystals whose primary particle has an average size of 0.1 to 5 microns.

7. A dentifrice composition according to claim 2 wherein the calcium hydrogenphosphate anhydride is spherulitic.

8. A toothpaste composition, comprising:

5 to 95% by weight of the composition of a calcium hydrogenphosphate anhydride abrasive whose crystallite has an average size of 300 to 3,500 angstroms as measured by X-ray diffractometry wherein the calcium hydrogenphosphate anhydride ha a density of 2.650 to 2.885 g/cm.sup.3, a specific surface area o 2.5 to 20 m.sup.2 /g as measured by the BET method, and an averag agglomerate diameter of 2 to 30 microns.

9. A dentifrice composition according to claim 8, wherein said abrasive is present in an amount of 10 to 90% by weight of the composition.

10. A method for cleaning teeth, comprising the steps of: applyin the dentifrice composition of claim 1 to a tooth surface; and scrubbing the tooth surface.

11. A dentifrice composition, comprising;

5 to 95% by weight of a calcium hydrogenphosphate anhydride abrasive whose crystallite has an average size of 300 to 3,500 angstroms as measured by X-ray diffractometry; and

at least one other ingredient selected from the group consisting of a binder, a humectant and a flavoring agent.

12. A dentifrice composition according to claim 11, which contain 0.1 to 5% by weight of the composition of a binder.

13. A dentifrice composition according to claim 11, which contain 1 to 70% by weight of the composition of a humectant.

14. A dentifrice composition according to claim 11, which contain 0.1 to 5% by weight of the composition of a flavoring agent.

15. A dentifrice composition according to claim 11, which contain magnesium tertiary phosphate.

16. A dentifrice composition according to claim 15, wherein said magnesium tertiary phosphate is present in an amount of 0.1 to 5% by weight of the composition.

L17: Entry 49 of 50 File: USPT

DOCUMENT-IDENTIFIER: US 4587120 A
TITLE: Oral composition and abrasive therefor

Brief Summary Text (2):
This invention relates to an abrasive for use in oral compositions such as dentifrices, prophylactic pastes and the like. More particularly, this invention relates to a highly cleaning, low abrading abrasive for use in oral compositions which consists of calcium hydrogenphosphate anhydride (secondary calcium phosphate anhydride) whose crystallite has an average size of 300 to 3,500 angstroms as measured by X-ray diffractometry. This invention also relates to an oral composition containing the abrasive.

Brief Summary Text (8):
As a result of extensive investigations to meet the above-mentioned need, the inventors have found that calcium hydrogenphosphate anhydri (secondary calcium phosphate anhydride) whose crystallite has an average size of 300 to 3,500 angstroms as measured by X-ray diffractome and preferably, which has a density of 2.650 to 2.885 grams per cubic centimeters, a specific surface area of 2.5 to 20 square meters per gram measured by the BET (Brunauer-Emmett-Teller) method, and an average agglomerate diameter of 2 to 30 micronmeters has good physical properties as an abrasive, and that when the above-defined calcium hydrogenphosphate anhydride is used as an abrasive in an oral compositi the resulting oral composition is improved in cleaning action and in the effect of making the tooth aesthetically white without increasing its abrasiveness.

Brief Summary Text (10):
It is well known in the art to use calcium hydrogenphosphate anhydride (secondary calcium phosphate anhydride) as an abrasive for dentific or the like. However, such previously used calcium hydrogenphosphate anhydride usually has an average crystallite size of 3,800 to 4,300 angstroms as measured by X-ray diffractometry, a specific surface area of about 1 to 2 m.sup.2 /g as measured by the BET method, and a density of 2.890 g/cm.sup.3 and has a microscopic-structure (a particle shape) as shown in FIG. 1, and as a result, exhibits too high abrasive as shown in experiments to be described later as long as it is in the form of single particle having a normal particle size, that is, a particle diameter of 10 to 30 microns. When such conventional calcium hydrogenphosphate anhydride is used alone as an abrasive, the resulting oral composition will show an abrasiveness value of above 250, as measured by the RDA (Radio Active Dentin Abrasion) method, which value i generally regarded as the upper limit by the ADA (American Dental Association) and other dental associations, and thus has the possibility o inducing wedgeshaped defects after long term repeated use if the brushing way is inadequate. For this reason, the conventional calcium hydrogenphosphate anhydride abrasive was used in combination with other mild abrasives. As compared with the conventional ones, the calcium hydrogenphosphate anhydride (secondary calcium phosphate anhydride) of the present invention has an average crystallite size of 3 to 3,500 angstroms as measured by X-ray diffractometry, has less sharp edges or more round edges, exhibits extremely low abrading action s that it can be used as a sole abrasive, and exhibits more cleaning action (or stain removing action) than other types of abrasive having a simil degree of abrasiveness, with the additional benefit of making the tooth aesthetically white. These are new findings made by the inventors.

Detailed Description Text (2):
The abrasive for use in oral compositions according to the present invention consists of calcium hydrogenphosphate anhydride (secondary calcium phosphate anhydride) whose crystallite has an average size (also referred to as "average crystallite size" herein) of 300 to 3,500 angstroms as measured by X-ray diffractometry as will be demonstrated in the experiment shown below, and which has a microscopic structu as shown in FIGS. 2-5. Because of its crystalline attributes, the calcium hydrogenphosphate anhydride of the invention exhibits a moderate degree of abrasiveness and a high degree of cleaning to the tooth, and at the same time, is effective for making the tooth aesthetically white.

Detailed Description Text (13):
The calcium hydrogenphosphate anhydride useful in the present invention may also include a spherulitic calcium hydrogenphosphate anhydr as shown in FIG. 5. This spherulitic calcium hydrogenphosphate anhydride is comparable in cleaning action to conventional abrasives havin abrasivity on copper plate of about 20 to 30 mg when it has an abrasivity on copper plate of about 1 to 5 mg, and to other conventional abrasives having the abrasivity of about 30 to 50 mg when it has the abrasivity of about 5 to 20 mg, as will be seen in experiments to be described later. In addition to such a unique combination of low abrasiveness with high cleanability, the spherulitic calcium hydrogenphosph anhydride has an improved lustering effect so that sufficient luster is imparted to the tooth surface even when it is used alone as an abrasive. compared with oral compositions containing a conventional subangular calcium hydrogenphosphate anhydride abrasive consisting of a mixtu

of plate, prism and needle crystals, oral compositions containing this spherulitic calcium hydrogenphosphate anhydride give little gritty feel the oral cavity, is mild to the oral membrane, and thus give a pleasant feel to the mouth. Namely, the use of spherulitic calcium hydrogenphosphate anhydride can meet the requirements of high cleanability, low abrasiveness, high lustering, and pleasant feel at the same time. The conventional prior art calcium hydrogenphosphate anhydride having an average agglomerate size of 10 to 30 microns is of a subangular shape as shown in FIG. 1 and has a roundness of about 0.4 and a specific surface area of about 1 to 2 m.sup.2 /g as measured by BET method, and thus exhibits too high abrading action as shown in experiments to be described later as long as it is in the form of agglomerates having a normal particle size. When such conventional one is used alone as a sole abrasive, the resulting oral composition will show an abrasion value of above 250 as measured by the RDA method and thus may induce wedge-shaped defects after long term repeated u as described above. On the other hand, the spherulitic calcium hydrogenphosphate anhydride of the present invention exhibits increased cleaning action irrespective of reduced abrasiveness and is effective for imparting luster to the tooth surface at the same time.

Detailed Description Text (19):
In the case of a dentifrice composition, for example, the calcium hydrogenphosphate anhydride (secondary calcium phosphate anhydride) abrasive of the present invention may be used alone or in admixture with any other conventional abrasives, for example, calcium hydrogenphosphate dihydrate, conventional calcium hydrogenphosphate anhydride having an average crystallite size of 3,800 to 4,300 angstroms (falling outside the scope of the invention), calcium carbonate, calcium pyrophosphate, insoluble sodium metaphosphate, amorph silica, crystalline sillica, precipitated silica, aluminosilicate, aluminum oxide, aluminum hydroxide, microcrystalline cellulose, resin, magnes tertiary phosphate, magnesium carbonate, etc. and mixtures thereof. When the calcium hydrogenphosphate anhydride of the present inventio combined with another abrasive or abrasives, the amount of the present phosphate used may preferably range from 5 to 100% by weight, mo preferably from 10 to 100% by weight of the combined abrasives for taking the substantial advantage of the present phosphate.

Detailed Description Text (21):
In an oral composition such as a dentifrice composition, the content of the abrasive may be in the range of 5 to 95% by weight, preferably 10 90% by weight of the composition. The content of the binder may be in the range of 0.1 to 5% by weight, preferably 0.3 to 3% by weight of composition. The content of the humectant may be in the range of 1 to 70% by weight, preferably 10 to 60% by weight of the composition. T content of the foaming agent may be in the range of 0.1 to 10% by weight, preferably 0.2 to 5% by weight of the composition. The content o the flavor may be in the range of 0.1 to 5% by weight, preferably 0.3 to 2% by weight of the composition. The content of the sweetner may b the range of 0.001 to 5% by weight, preferably 0.005 to 2% by weight of the composition.

Detailed Description Text (53):
The following clinical test was carried out to demonstrate how a dentifrice containing the calcium hydrogenphosphate anhydride abrasive of invention is effective for making the tooth aesthetically white.

Detailed Description Text (58):
Using these criteria, the degree of stain on teeth was evaluated in terms of (I) multiplied by (II) for each tooth. It will be readily understood t for each tooth, the worst point is 10.times.3=30 points. The result for each toothpaste is expressed as an average value per tooth.

Detailed Description Text (61):
Another clinical test was carried out to demonstrate how a dentifrice containing the calcium hydrogenphosphate anhydride abrasive of the invention is effective for making the tooth aesthetically white.

Detailed Description Text (63):
A number of smokers who had brushed their teeth with an abrasive-free dentifrice for one month and thus had their teeth stained were classif into three panels such that each panel consisted of 14 smokers and the average value of stain was substantially the same among the panels. T brushed for a further three weeks with the toothpaste of the above-mentioned formulation. The stain of teeth was evaluated before and after t tooth stain, five examiners examined the front and rear surfaces of upper two and lower two anteriors in accordance with the following criter The stain was expressed as an average point per tooth for each panel member

Detailed Description Text (75):
A further clinical test was carried out to demonstrate how a dentifrice containing the calcium hydrogenphosphate anhydride abrasive of the invention is effective for making the tooth aesthetically white.

Detailed Description Text (93):
Ten panel members held one-half cup of noncarbonated, pure orange juice in their mouth some time and then swallowed it down such that th perceived the taste or feel of the juice. Then, they brushed their tooth with the above-prepared toothpaste, and drank the same cup of juice in same manner as above one minute after the tooth-brushing. A change of taste was evaluated in accordance with the following criterion. The results, which are expressed as a total of the respective points that ten members gave for each toothpaste, are shown in Table 14.

Detailed Description Text (96):
The data of Table 14 prove that the toothpaste containing the abrasive of the present invention exhibits improved juice effect and gives a pleasant feel to the mouth. That is, the toothpaste of formulation J having the abrasive of the invention blended therein is significantly impro

in juice effect and more favored than that of formulation K having prior art calcium hydrogenphosphate anhydride blended therein and that o formulation L having N-lauroylsarcosinate blended in formulation K, and substantially equivalent in juice effect and favorableness to that of formulation M having .alpha.-olefin sulfonate blended therein as a foaming agent.

Detailed Description Text (117):
As seen from the data of Table 21, the toothpaste having the spherulitic calcium hydrogenphosphate anhydride abrasive blended therein is m favorable than the toothpaste having the prior art calcium hydrogenphosphate anhydride abrasive blended therein. Fourteen members among panel members reported that the former toothpaste is milder to the mouth. That is, the spherulitic calcium hydrogenphosphate anhydride abrasive of the present invention is improved in oral cavity cleaning action and gives a more pleasant feel to the mouth irrespective of low abrasiveness as compared with the prior art calcium hydrogenphosphate anhydride abrasive.

Detailed Description Paragraph Table (21):
__________________________________ Evaluation criterion As compared with the former toothpaste used in brushing, the latter toothpaste is __________________________________ +2: much favorable. +1: appreciably favorable. 0: equally favorable. -1: somew unfavorable. -2: strongly unfavorable. __________________________________

Detailed Description Paragraph Table (30):
TABLE 21 __________________________________ Number of panel members Mixing favor- Unfavor- No differ- Abrasive ratio ab able ence __________________________________ DCP-D No. 2/ 5/5 6 7 7 Com- DCP-A No. 4 parison DCP-D No. 2/ 5/5 13 3 4 In- DCP-A No. 28 vention __________________________________ Note: The tests total to 40 since the order effect is taken into accoun that is, one toothpaste is followed by the other in the first test and the other is followed by the one in the second test.

CLAIMS:

1. A dentifrice composition comprising an abrasive consisting of calcium hydrogenphosphate anhydride whose crystallite has an average siz 300 to 3,500 angstroms as measured by X-ray diffractometry.

2. A dentifrice composition according to claim 1 wherein the calcium hydrogenphosphate anhydride has a density of 2.650 to 2.885 g/cm.sup a specific surface area of 2.5 to 20 m.sup.2 /g as measured by the BET method, and an average agglomerate diameter of 2 to 30 microns.

3. A dentifrice composition according to claim 1 wherein the calcium hydrogenphosphate anhydride is in the form of a cohesive aggregate o plate crystals whose primary particle has an average size of 0.1 to 5 microns.

4. A dentifrice composition according to claim 1 wherein the calcium hydrogenphosphate anhydride is spherulitic.

5. A dentifrice composition according to claim 4 wherein the spherulitic calcium hydrogenphosphate anhydride has an average roundness of 0.45 to 0.9.

6. A dentifrice composition according to claim 2 wherein the calcium hydrogenphosphate anhydride is in the form of a cohesive aggregate o plate crystals whose primary particle has an average size of 0.1 to 5 microns.

7. A dentifrice composition according to claim 2 wherein the calcium hydrogenphosphate anhydride is spherulitic.

8. A toothpaste composition, comprising:

9. A dentifrice composition according to claim 8, wherein said abrasive is present in an amount of 10 to 90% by weight of the composition.

10. A method for cleaning teeth, comprising the steps of: applying the dentifrice composition of claim 1 to a tooth surface; and scrubbing the tooth surface.

11. A dentifrice composition, comprising;

12. A dentifrice composition according to claim 11, which contains 0.1 to 5% by weight of the composition of a binder.

13. A dentifrice composition according to claim 11, which contains 1 to 70% by weight of the composition of a humectant.

14. A dentifrice composition according to claim 11, which contains 0.1 to 5% by weight of the composition of a flavoring agent.

15. A dentifrice composition according to claim 11, which contains magnesium tertiary phosphate.

16. A dentifrice composition according to claim 15, wherein said magnesium tertiary phosphate is present in an amount of 0.1 to 5% by weig

of the composition.

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L17: Entry 49 of 50 File: USPT May 6, 1986

US-PAT-NO: 4587120
DOCUMENT-IDENTIFIER: US 4587120 A

TITLE: Oral composition and abrasive therefor

DATE-ISSUED: May 6, 1986

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ozawa; Toshiyuki	Chigasaki			JP
Uotani; Osamu	Chiba			JP
Hayashi; Rieko	Odawara			JP

ASSIGNEE-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY	TYPE CODE
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APPL-NO: 06/ 566681 [PALM]
DATE FILED: December 29, 1983

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	APPL-DATE
JP	57-228601	December 29, 1982
JP	57-228602	December 29, 1982

INT-CL: [04] A61K 7/16

US-CL-ISSUED: 424/57; 424/49
US-CL-CURRENT: 424/57; 424/49

FIELD-OF-SEARCH: 424/57

PRIOR-ART-DISCLOSED:

U.S. PATENT DOCUMENTS

Search Selected | Search ALL

PAT-NO	ISSUE-DATE	PATENTEE-NAME	US-CL
2018410	October 1935	McDonald et al.	424/57
4108961	August 1978	Ploger et al.	424/57
4108962	August 1978	Ploger et al.	424/57
4130630	December 1978	Ploger et al.	424/57

FOREIGN PATENT DOCUMENTS

FOREIGN-PAT-NO	PUBN-DATE	COUNTRY	US-CL
53-124631	October 1978	JP	424/57

ART-UNIT: 123

PRIMARY-EXAMINER: Rose; Shep K.

ABSTRACT:

Calcium hydrogenphosphate anhydride is disclosed whose crystallite has an average size of 300 to 3,500 angstroms as measured by X-ray diffractometry, and preferably, which has a density of 2.650 to 2.885 grams per cubic centimeters, a specific surface area of 2.5 to 20 square meters per gram as measured by the BET method, and an average agglomerate diameter of 2 to 30 micronmeters has good physical propertie an abrasive, and that when it is used as an abrasive in an oral composition, the resulting oral composition is improved in cleaning action and the effect of making the tooth aesthetically white without increasing its abrasiveness.

16 Claims, 10 Drawing figures

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L17: Entry 48 of 50 File: USPT

US-PAT-NO: 4743274
DOCUMENT-IDENTIFIER: US 4743274 A

TITLE: Oral composition and abrasive therefor

DATE-ISSUED: May 10, 1988

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ozawa; Toshiyuki	Chigasaki			JP
Uotani; Osamu	Chiba			JP
Hayashi; Rieko	Odawara			JP

US-CL-CURRENT: 51/309; 424/57

CLAIMS:

What is claimed is:

1. An abrasive suitable for use in dentrifrice compositions consisting of calcium hydrogenphosphate anhydride whose crystallite has an average size of 300 to 3,500 angstroms as measured by X-ray diffractometry.

2. An abrasive suitable for use in dentifrice compositions according to claim 1 wherein the calcium hydrogenphosphate anhydride has a density of 2.650 to 2.885 g/cm.sup.3, a specific surface area of 2.5 to 20 m.sup.2 /g as measured by the BET method, and an average agglomerate diameter of 2 to 30 microns.

3. An abrasive suitable for use in dentifrice compositions according to claim 1 wherein the calcium hydrogenphosphate anhydride is in the form of a cohesive aggregate of plate crystal whose primary particle has an average size of 0.1 to 5 microns.

4. An abrasive suitable for use in dentifrice compositions according to claim 1 wherein the calcium hydrogenphosphate anhydride is spherulitic.

5. An abrasive suitable for use in dentifrice compositions according to claim 4 wherein the spherulitic calcium hydrogenphosphate anhydride has an average roundness of 0.45 to

0.9.

6. An abrasive suitable for use in dentifrice compositions according to claim 2, wherein the calcium hydrogenphosphate anhydride is in the form of a cohesive aggregate of plate cyrstal whose primary particle has an average size of 0.1 to 5 microns.

7. An abrasive suitable for use in dentifrice compositions according to claim 2, wherein the calcium hydrogenphosphate anhydride is spherulitic.

8. An abrasive suitable for use in oral compositions according to claim 1, wherein the calcium hydrogenphosphate anhydride has a density of 2.650 to 2.885 g/cm.sup.3.

9. An abrasive suitable for use in oral compositions according to claim 1, wherein the calcium hydrogenphosphate anhydride has a specific surface area of 2.5 to 20 m.sup.2 /g as measured by the BET method.

10. An abrasive suitable for use in oral compositions according t claim 1, wherein the calcium hydrogenphosphate anhydride has an average agglomerate diameter of 2 to 30 microns.

11. The abrasive of claim 1, which is prepared by reacting phosphoric acid with a suspension of calcium hydroxide and water in the presence of a crystallization modifier capable of controlling the growth of crystals.

12. The abrasive of claim 11, wherein the crystallization modifie is a phosphoric acid condensate.

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L17: Entry 48 of 50 File: USPT

DOCUMENT-IDENTIFIER: US 4743274 A
TITLE: Oral composition and abrasive therefor

Brief Summary Text (2):
This invention relates to an abrasive for use in oral compositions such as dentrifrices, prophylactic pastes and the like. More particularly, thi invention relates to a highly cleaning, low abrading abrasive for use in oral compositions which consists of calcium hydrogenphosphate anhydride (secondary calcium phosphate anhydride) whose crystallite has an average size of 300 to 3,500 angstroms as measured by X-ray diffractometry. This invention also relates to an oral composition containing the abrasive.

Brief Summary Text (8):
As a result of extensive investigations to meet the above-mentioned need, the inventors have found that calcium hydrogenphosphate anhydri (secondary calcium phosphate anhydride) whose crystallite has an average size of 300 to 3,500 angstroms as measured by X-ray diffractome and preferably, which has a density of 2.650 to 2.885 grams per cubic centimeters, a specific surface area of 2.5 to 20 square meters per gram measured by the BET (Brunauer-Emmett-Teller) method, and an average agglomerate diameter of 2 to 30 micronmeters has good physical properties as an abrasive, and that when the above-defined calcium hydrogenphosphate anhydride is used as an abrasive in an oral compositi the resulting oral composition is improved in cleaning action and in the effect of making the tooth aesthetically white without increasing its abrasiveness.

Brief Summary Text (10):
It is well known in the art to use calcium hydrogenphosphate anhydride (secondary calcium phosphate anhydride) as an abrasive for dentrific or the like. However, such previously used calcium hydrogenphosphate anhydride usually has an average crystallite size of 3,800 to 4,300 angstroms as measured by X-ray diffractometry, a specific surface area of about 1 to 2 m.sup.2 /g as measured by the BET method, and a density of 2.890 g/cm.sup.3 and has a microscopic-structure (a particle shape) as shown in FIG. 1, and as a result, exhibits too high abrasive as shown in experiments to be described later as long as it is in the form of single particle having a normal particle size, that is , a particle diameter of 10 to 30 microns. When such conventional calcium hydrogenphosphate anhydride is used alone as an abrasive, the resulting oral composition will show an abrasiveness value of above 250, as measured by the RDA (Radio Active Dentin Abrasion) method, which value i generally regarded as the upper limit by the ADA (American Dental Association) and other dental associations, and thus has the possibility o inducing wedgeshaped defects after long term repeated use if the brushing way is inadequate. For this reason, the conventional calcium hydrogenphosphate anhydride abrasive was used in combination with other mild abrasives. As compared with the conventional ones, the calcium hydrogenphosphate anhydride (secondary calcium phosphate anhydride) of the present invention has an average crystallite size of 3 to 3,500 angstroms as measured by X-ray diffractometry, has less sharp edges or more round edges, exhibits extremely low abrading action s that it can be used as a sole abrasive, and exhibits more cleaning action (or stain removing action) than other types of abrasive having a simil degree of abrasiveness, with the additional benefit of making the tooth aesthetically white. These are new findings made by the inventors.

Detailed Description Text (2):
The abrasive for use in oral compositions according to the present invention consists of calcium hydrogenphosphate anhydride (secondary calcium phosphate anhydride) whose crystallite has an average size (also referred to as "average crystallite size" herein) of 300 to 3,500 angstroms as measured by X-ray diffractometry as will be demonstrated in the experiment shown below, and which has a microscopic structu as shown in FIGS. 2-5. Because of its crystalline attributes, the calcium hydrogenphosphate anhydride of the invention exhibits a moderate degree of abrasiveness and a high degree of cleaning to the tooth, and at the same time, is effective for making the tooth aesthetically white.

Detailed Description Text (13):
The calcium hydrogenphosphate anhydride useful in the present invention may also include a spherulitic calcium hydrogenphosphate anhydr as shown in FIG. 5. This spherulitic calcium hydrogenphosphate anhydride is comparable in cleaning action to conventional abrasives havin arbrasivity on copper plate of about 20 to 30 mg when it has an abrasivity on copper plate of about 1 to 5 mg, and to other conventional abrasives having the abrasivity of about 30 to 50 mg when it has the abrasivity of about 5 to 20 mg, as will be seen in experiments to be described later. In addition to such a unique combination of low abrasiveness with high cleanability, the spherulitic calcium hydrogenphosph anhydride has an improved lustering effect so that sufficient luster is imparted to the tooth surface even when it is used alone as an abrasive. compared with oral compositions containing a conventional subangular calcium hydrogenphosphate anhydride abrasive consistig of a mixtur

of plate, prism and needle crystals, oral compositions containing this spherulitic calcium hydrogenphosphate anhydride give little gritty feel the oral cavity, is mild to the oral membrane, and thus give a pleasant feel to the mouth. Namely, the use of spherulitic calcium hydrogenphosphate anhydride can meet the requirements of high cleanability, low abrasiveness, high lustering, and pleasant feel at the same time. The conventional prior art calcium hydrogenphosphate anhydride having an average agglomerate size of 10 to 30 microns is of a subangular shape as shown in FIG. 1 and has a roundness of about 0.4 and a specific surface area of about 1 to 2 m.sup.2 /g as measured by BET method, and thus exhibits too high abrading action as shown in experiments to be described later as long as it is in the form of agglomerates having a normal particle size. When such conventional one is used alone as a sole abrasive, the resulting oral composition will show an abrasion value of about 250 as measured by the RDA method and thus may induce wedge-shaped defects after long term repeated u as described above. On the other hand, the spherulitic calcium hyrogenphosphate anhydride of the present invention exhibits increased clean action irrespective of reduced abrasiveness and is effective for imparting luster to the tooth surface at the same time.

Detailed Description Text (19):
In the case of a dentifice composition, for example, the calcium hydrogenphosphate anhydride (secondary calcium phosphate anhydride) abrasive of the present invention may be used alone or in admixture with any other conventional abrasives, for example, calcium hydrogenphosphate dihydrate, conventional calcium hydrogenphosphate anhydride having an average crystallite size of 3,800 to 4,300 angstroms (falling outside the scope of the invention), calcium carbonate, calcium pyrophosphate, insoluble sodium metaphosphate, amorph silica, crystalline silica, precipitated silica, aluminosilicate, aluminum oxide, aluminum hydroxide, microcrystalline cellulose, resin, magnesi tertiary phosphate, magnesium carbonate, etc. and mixtures thereof. When the calcium hydrogenphosphate anhydride of the present inventio combined with another abrasive or abrasives, the amount of the present phosphate used may preferably range from 5 to 100% by weight, mo preferably from 10 to 100% by weight of the combined abrasives for taking the substantial advantage of the present phosphate.

Detailed Description Text (21):
In an oral composition such as a dentifrice composition, the content of the abrasive may be in the range of 5 to 95% by weight, preferably 10 90% by weight of the composition. The content of the binder may be in the range of 0.1 to 5% by weight, preferably 0.3 to 3% by weight of composition. The content of the humectant may be in the range of 1 to 70% by weight, preferably 10 to 60% by weight of the composition. T content of the foaming agent may be in the range of 0.1 to 10% by weight, preferably 0.2 to 5% by weight of the composition. The content o the flavor may be in the range of 0.1 to 5% by weight, preferably 0.3 to 2% by weight of the composition. The content of the sweetner may b the range of 0.001 to 5% by weight, preferably 0.005 to 2% by weight of the composition.

Detailed Description Text (53):
The following clinical test was carried out to demonstrate how a dentifrice containing the calcium hydrogenphosphate anhydride abrasive of invention is effective for making the tooth aesthetically white.

Detailed Description Text (60):
Using these criteria, the degree of stain on teeth was evaluated in terms of (I) multiplied by (II) for each tooth. It will be readily understood t for each tooth, the worst point is 10.times.3=30 points. The result for each toothpaste is expressed as an average value per tooth.

Detailed Description Text (63):
Another clinical test was carried out to demonstrate how a dentifrice containing the calcium hydrogenphosphate anhydride abrasive of the invention is effective for making the tooth aesthetically white.

Detailed Description Text (65):
A number of smokers who had brushed their teeth with an abrasive-free dentifrice for one month and thus had their teeth stained were classif into three panels such that each panel consisted of 14 smokers and the average value of stain was substantially the same among the panels. T brushed for a further three weeks with the toothpaste of the above-mentioned formulation. The stain of teeth was evaluated before and after t tooth stain, five examiners examined the front and rear surfaces of upper two and lower two anteriors in accordance with the following criter The stain was expressed as an average point per tooth for each panel member.

Detailed Description Text (77):
A further clinical test was carried out to demonstrate how a dentifrice containing the calcium hydrogenphosphate anhydride abrasive of the invention is effective for making the tooth aesthetically white.

Detailed Description Text (94):
Ten panel members held one-half cup of noncarbonated, pure orange juice in their mouth some time and then swallowed it down such that th perceived the taste or feel of the juice. Then, they brushed their tooth with the above-prepared toothpaste, and drank the same cup of juice in same manner as above one minute after the tooth-brushing. A change of taste was evaluated in accordance with the following criterion. The results, which are expressed as a total of the respective points that ten members gave for each toothpaste, are shown in Table 14

Detailed Description Text (102):
As compared with the former toothpaste used in brushing, the latter toothpaste is

Detailed Description Text (108):
The data of Table 14 proves that the toothpaste containing the abrasive of the present invention exhibits improved juice effect and gives a pleasant feel to the mouth. That is, the toothpaste of formulation J having the abrasive of the invention blended therein is significantly impro in juice effect and more favored than that of formulation K having prior art calcium hydrogenphosphate anhydride blended therein and that o formulation L having N-lauroylsarcosinate blended in formulation K, and substantially equivalent in juice effect and favorableness to that of formulation M having .alpha.-olefin sulfonate blended therein as a foaming agent.

Detailed Description Text (128):
As seen from the data of Table 21, the toothpaste having the spherulitic calcium hydrogenphosphate anhydride abrasive blended therein is m favorable than the toothpaste having the prior art calcium hydrogenphosphate anhydride abrasive blended therein. Fourteen members among panel members reported that the former toothpaste is milder to the mouth. That is, the spherulitic calcium hydrogenphosphate anhydride abrasive of the present invention is improved in oral cavity cleaning action and gives a more pleasant feel to the mouth irrespective of low abrasiveness as compared with the prior art calcium hydrogenphosphate anhydride abrasive.

Detailed Description Paragraph Table (29):
TABLE 21 ______________________________________ Number of panel members Un- No Mixing favor- favor- differ- Abrasive ratio a able ence ______________________________________ DCP-D No. 2/ 5/5 6 7 7 Compari- DCP-A No. 4 son DCP-D No. 2/ 5/5 13 3 4 Invention DCP-A No. 28 ______________________________________ Note: The tests total to 40 since the order effect is taken into acco that is, one toothpaste is followed by the other in the first test and the other is followed by the one in the second test.

CLAIMS:

1. An abrasive suitable for use in dentifrice compositions consisting of calcium hydrogenphosphate anhydride whose crystallite has an avera size of 300 to 3,500 angstroms as measured by X-ray diffractometry.

2. An abrasive suitable for use in dentifrice compositions according to claim 1 wherein the calcium hydrogenphosphate anhydride has a dens of 2.650 to 2.885 g/cm.sup.3, a specific surface area of 2.5 to 20 m.sup.2 /g as measured by the BET method, and an average agglomerate diameter of 2 to 30 microns.

3. An abrasive suitable for use in dentifrice compositions according to claim 1 wherein the calcium hydrogenphosphate anhydride is in the fo of a cohesive aggregate of plate crystals whose primary particle has an average size of 0.1 to 5 microns.

4. An abrasive suitable for use in dentifrice compositions according to claim 1 wherein the calcium hydrogenphosphate anhydride is spherul

5. An abrasive suitable for use in dentifrice compositions according to claim 4 wherein the spherulitic calcium hydrogenphosphate anhydride has an average roundness of 0.45 to 0.9.

6. An abrasive suitable for use in dentifrice compositions according to claim 2, wherein the calcium hydrogenphosphate anhydride is in the f of a cohesive aggregate of plate cyrstals whose primary particle has an average size of 0.1 to 5 microns.

7. An abrasive suitable for use in dentifrice compositions according to claim 2, wherein the calcium hydrogenphosphate anhydride is spherul

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L17: Entry 48 of 50 File: USPT May 10, 1988

US-PAT-NO: 4743274
DOCUMENT-IDENTIFIER: US 4743274 A

TITLE: Oral composition and abrasive therefor

DATE-ISSUED: May 10, 1988

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ozawa; Toshiyuki	Chigasaki			JP
Uotani; Osamu	Chiba			JP
Hayashi; Rieko	Odawara			JP

ASSIGNEE-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY	TYPE CODE
Lion Corporation	Tokyo			JP	03

APPL-NO: 06/ 824198 [PALM]
DATE FILED: January 30, 1986

PARENT-CASE:
This application is a division of application Ser. No. 566,681, filed Dec. 29, 1983, now U.S. Pat. No. 4,587,120.

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	APPL-DATE
JP	57-228601	December 29, 1982
JP	57-228602	December 29, 1982

INT-CL: [04] B24D 3/02

US-CL-ISSUED: 51/309; 424/57
US-CL-CURRENT: 51/309; 424/57

FIELD-OF-SEARCH: 424/57, 51/309

PRIOR-ART-DISCLOSED:

U.S. PATENT DOCUMENTS

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	PAT-NO	ISSUE-DATE	PATENTEE-NAME	US-CL
☐	2018410	October 1935	McDonald et al.	167/93
☐	3012852	December 1961	Nelson	424/57
☐	3066056	November 1962	Schlaeger et al.	424/57
☐	3169096	February 1965	Schlaeger et al.	424/57
☐	3647371	March 1972	Kim et al.	424/57
☐	3829562	August 1974	Kim et al.	424/57
☐	4038380	July 1977	Cordon	51/309
☐	4108961	August 1978	Ploger et al.	424/57
☐	4108962	August 1978	Ploger et al.	424/57
☐	4130630	December 1978	Ploger et al.	424/57
☐	4244707	January 1981	Wason	51/309
☐	4280822	July 1981	Wason	51/309
☐	4444570	April 1984	Barth et al.	51/309
☐	4587120	May 1986	Ozawa et al.	424/57

FOREIGN PATENT DOCUMENTS

FOREIGN-PAT-NO	PUBN-DATE	COUNTRY	US-CL
47-2431	January 1972	JP	
53-124631	October 1978	JP	

ART-UNIT: 115

PRIMARY-EXAMINER: Clingman; A. Lionel

ASSISTANT-EXAMINER: Thompson; Willie J.

ABSTRACT:

Calcium hydrogenphosphate anhydride is disclosed whose crystallite has an average size of 300 to 3,500 angstroms as measured by X-ray diffractometry, and preferably, which has a density of 2.650 to 2.885 grams per cubic centimeters, a specific surface area of 2.5 to 20 square meters per gram as measured by the BET method, and an average agglomerate diameter of 2 to 30 micronmeters has good physical propertie an abrasive, and that when it is used as an abrasive in an oral composition, the resulting oral composition is improved in cleaning action and the effect of making the tooth aesthetically white without increasing its abrasiveness.

12 Claims, 10 Drawing figures

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DENTIFRICE.DWPI,TDBD,EPAB,JPAB,USPT.	5748
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(10 AND (DENTIFRICE OR TOOTHPASTE)).USPT,JPAB,EPAB,DWPI,TDBD.	50
(L10 AND (DENTIFRICE OR TOOTHPASTE)).USPT,JPAB,EPAB,DWPI,TDBD.	50

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L17	l10 and (dentifrice or toothpaste)	50	L17
L16	l3 and (dentifrice or toothpaste)	0	L16
L15	l3 and stomatol?	0	L15
L14	l13 and (surfactant? or surface active agent? or wetting agent? or protective colloid?)	22	L14
L13	l11 and agglomerat?	37	L13
L12	l11 and particle?.clm.	126	L12
L11	l10 and (nano?.clm. or nm.clm. or nanometers.clm. or nanometer?.clm.)	416	L11
L10	l1 and (whiskers or rodlike or barlike or needle crystals or particle length? or nanometers or nanocrystals or nanoparticles or rod-shaped or bar-shaped or 20nm or 70 nm or 5 nm or 10 nm or 40 nm or 50 nm or 35 nm or 30 nm or 130 nm or 50 nanometers or 150 nanometers)	3756	L10
L9	l8 and diameter? and length?	12	L9
L8	l3 and (toothpaste or dentifrice or stomatol? or teeth or dental)	48	L8
L7	l5 and l2	0	L7
L6	l5 and nano?.clm.	0	L6
L5	l1 and nano?	35	L5
L4	l3 and crystals and particle size	32	L4
L3	l1 and (anisometric or anisotropic)	307	L3
L2	l1 and agglomeration	879	L2
L1	(calcium phosphate or apatite or hydroxylapatite or hydroxyapatite or calcium fluoride or fluorapatite o0r amorphous calcium phosphate or fluorophosphate calcium or calcium fluorophosphate or fluorine-doped hydroxylapatite or f-doped hydroxylapatite)	47239	L1

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L13	l11 and agglomerat?	37	L13
L12	l11 and particle?.clm.	126	L12
L11	l10 and (nano?.clm. or nm.clm. or nanometers.clm. or nanometer?.clm.)	416	L11
L10	l1 and (whiskers or rodlike or barlike or needle crystals or particle length? or nanometers or nanocrystals or nanoparticles or rod-shaped or bar-shaped or 20nm or 70 nm or 5 nm or 10 nm or 40 nm or 50 nm or 35 nm or 30 nm or 130 nm or 50 nanometers or 150 nanometers)	3756	L10
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L1	(calcium phosphate or apatite or hydroxylapatite or hydroxyapatite or calcium fluoride or fluorapatite o0r amorphous calcium phosphate or fluorophosphate calcium or calcium fluorophosphate or fluorine-doped hydroxylapatite or f-doped hydroxylapatite)	47239	L1

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Search: l10 and (dentifrice or toothpaste)

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L1	(calcium phosphate or apatite or hydroxylapatite or hydroxyapatite or calcium fluoride or fluorapatite o0r amorphous calcium phosphate or fluorophosphate calcium or calcium fluorophosphate or fluorine-doped hydroxylapatite or f-doped hydroxylapatite)	47239	L1

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